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JOURNAL OF THE BRITISH MEDICAL ASSOCIATION

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY SEPTEMBER 16 1961

PROTECTION OF THE RESPIRATORY TRACT*

BY

Sir VICTOR NEGUS, D.Sc., M.S., F.R.C.S.

[WITH SPECIAL PLATE]

The memory of Walter Jobson Horne will be kept alive by the institution of this lecture. I am proud to be the first to deliver it, particularly as I remember a number of meetings at which his somewhat controversial observations gave life to the discussions. He was in appearance rotund and reminiscent of a character from Dickens; in intellect he was erudite and a good speaker. He was, in brief, a character.

The respiratory tract, and particularly inflammatory lesions of the larynx, were of great interest to him; his inclination was toward pathology and away from operations, characteristics to be remembered and imitated. A keen supporter of the B.M.A. and President of a Section at the Meeting in Bradford, he also had the honour of giving the Semon Lecture in 1921.

I have chosen as my subject: "Protection of the Respiratory Tract."

Consideration of this problem allows no distinction to be drawn between the upper and lower respiratory passages, as frequently occurs in the education of medical students; the former is often classed as a special subject and the latter as part of general medicine, with confusing results.

Since infections of the respiratory tract are among the most common of complaints, with the loss of a vast number of working days, it is important to have some understanding of the complicated physiological processes entailed.

After a medical career devoted to the study of this subject I regret to find myself in some confusion, but I will attempt to outline certain aspects which I hope will serve as a basis for therapeutic principles.

The respiratory tract must be considered from the nostrils to the alveoli, and in addition the peculiar anatomy of man makes it essential to include the mouth and pharynx, since mouth-breathing is frequently used, especially during speech. It will be best to consider the various dangers against which protection must be afforded, and foremost among these is the avoidance of entry of water and food into the trachea and bronchi; this is a primitive function which concerns lung-breathing fish, amphibians, reptiles, birds, and mammals.

When the pulmonary apparatus was evolved it was essential to provide a protective valve at its origin from the pharynx; this valve is the larynx, often considered, incorrectly, to function solely as the organ of voice. Phonation is, however, facilitated in animals with a larynx, this being a convenient organ for the purpose, without anatomical adaptation. The simple larynx of an alligator, for example, lying flat in the floor of the pharynx, remains closed when water or food is being swallowed; reflex stimulation removes the danger of inundation of the trachea or lungs through an open glottis, and the same applies to the uncomplicated larynx of an amphibian such as the newt.

Crossing of the Air and Food Passages

Animals with a pulmonary apparatus inspire through the nose. This route is not designed for the benefit of respiration, but has as its object the drawing of air over the olfactory mucosa in order to maintain the acuity of the sense of smell. Since the nasal passages open in the roof of the mouth or pharynx, while the larynx opens from the floor of the pharynx, there is, of necessity, crossing of the two tracts for air and for food. In lung-fish, amphibians, reptiles, and birds it is essential that respiration shall cease while food and water are passing down the gullet; but in certain mammals the desirability of swallowing and breathing simultaneously has been overcome when the food is semi-liquid. This occurs with herbage, which must be taken in over lengthy periods of time (Text Fig. 1). Crossing of the passages for air and food is a particular cause of trouble in man.

Requirements of Olfaction

An important anatomical structure to be considered now is the epiglottis, which rises at the anterior end of the larynx; it is developed in animals of keen powers of scent to subserve the olfactory sense by its approximation to the soft palate, thereby shutting off the mouth from the air-stream and thus ensuring passage of all of the inspired air over the olfactory mucosa of the nose (Text Fig. 1).

The presence of the epiglottis does not of itself solve the problem of simultaneous breathing and swallowing; but a further modification connected with the epiglottis is of help. This modification is the lateral food-channel.

Lateral Food Channel

This channel is bounded medially by the aryteno-epiglottic fold and is shut off above by prolongation of the soft palate; this divides to form a shelf around the upstanding larynx, which projects into the posterior nasal passage; the food-passage is thereby separated

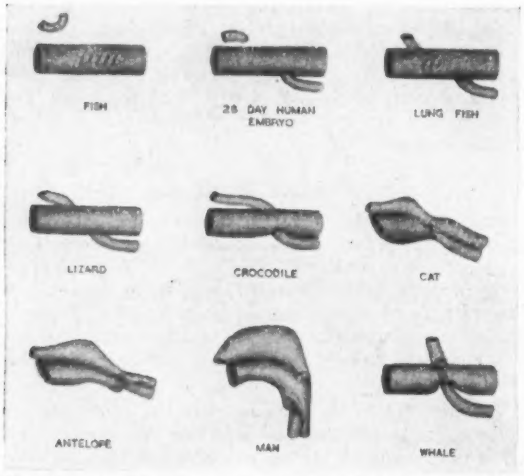
*The Walter Jobson Horne Memorial Lecture delivered at the Adjourned Annual General Meeting of the British Medical Association, Sheffield, July 20, 1961.

from the air-passages. In herbivorous animals such as deer and antelopes the channel is very efficient; the most efficient examples are found in cetaceans such as dolphins, porpoises, and some whales (Text Fig. 2).

Man, of herbivorous descent, has lateral food-passages of a sort along which liquids or semi-liquids may travel. These passages, though extremely efficient in true herbivora such as ungulates and many rodents, are in man not very effective in protecting the respiratory tract. It therefore happens that, though the infant can swallow milk along the lateral channels without complete interruption of respiration, the adult runs a risk if he attempts to swallow and breathe at the same time; it is common experience to find that fluid has gone the wrong way, and in individuals with paralysis of the larynx this experience is dangerous and sometimes fatal.

Entrance of Solid Objects

The inefficiency of the lateral passages is a danger to man as regards entrance of liquids, but a further hazard exists in his faculty of breathing through the mouth. The close apposition of epiglottis and soft palate of keen-scented animals is no longer required in higher apes and man, because of regression of the sense of smell in favour of sight. Evolutionary flexion of the head on the vertebral column with, in man, shortening of the snout leads to separation of the epiglottis from the palate, allowing air to pass freely through the mouth when it is open. This is, of course, to the advantage of speech, though it reduces the safety of the respiratory tract (Text Fig. 3). If some object is held between the lips or teeth, or is in the buccal cavity, a sudden inspiration may draw it through the larynx into the trachea or one of the bronchi; this applies especially to such light objects as pieces of nut or fragments of vegetables, substances which by irritative effects on the bronchial mucous membrane are very dangerous and often fatal. Sudden laughter or a cry may precipitate this accident.



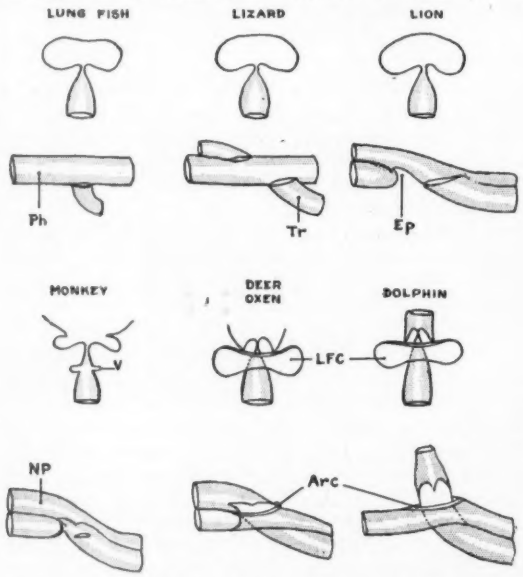
TEXT FIG. 1.—Diagram to illustrate modifications to subserve olfaction. In most gill-breathing fish there is no communication between the olfactory organ and the food-tract; the early human embryo is similar. In air-breathing lung-fish and in amphibians, reptiles, most birds, and all mammals the nasal passage opens into the mouth or pharynx. Coaptation of nasal and pulmonary air-passages is illustrated in the crocodile, cat, and antelope, the epiglottis of mammals assisting in this process. Man is seen to have a gap between nasal and pulmonary air-tracts. Cetaceans, such as some whales, have a permanently intranarial larynx, of great benefit for simultaneous breathing and swallowing.

Entrance of Bacteria

The larynx is incapable of preventing entrance of bacteria coming from the external air or from the nasal passages, the sinuses, or the pharynx; each respiration may carry in and out innumerable organisms, a strong reason for the wearing of a mask by those with respiratory infections. The nose itself, when infected, becomes a danger instead of a protection to the respiratory passages. It is most important, therefore, to deal effectively with inflammatory conditions of the nose, and especially with collections of pus in the paranasal cavities; the maxillary sinuses are usually the key to the situation, and puncture and lavage at an appropriate time may be indicated as a means of avoiding chronic infections or spread to other sinuses.

Stagnation of secretions in the posterior nasal passage, usually known as the nasopharynx, is frequently due to the obstructive presence of adenoids and can be of considerable danger; surgical clearance may be necessary, but with special care to avoid damaging submucosal tissues, such as the pharyngeal aponeurosis and muscle fibres, for fear of subsequent scarring and elimination of ciliary streams, leading to droplet infection of the lungs. Normally ciliary streams propel a mucoid blanket which is then carried by swallowing movements, starting in the posterior nasal passage, into the stomach, where organisms are killed by gastric juices.

Removal of adenoids is a difficult operation if it is to succeed in clearing obstruction without inflicting damage on the submucosa. Removal of tonsils, if it



TEXT FIG. 2.—Diagram to illustrate the lateral food-channel. In each case the pharynx and larynx are seen in transverse section above and laterally below. Ph=pharynx; Tr=trachea; Ep=epiglottis; V=laryngeal ventricle; LFC=lateral food-channel; NP=nasal passage; Arc=arcus palato-pharyngeus. The larynx of the lung-fish lies flat in the floor of the pharynx with no lateral protection; the arrangement in the lizard is similar, the glottis being at some distance from the nasal passage. In the lion there is an epiglottis for olfactory purposes, but no protection of the pulmonary air-passage except when the glottis is closed. The monkey has aryteno-epiglottic folds with a lateral food-channel of no great efficiency. Herbivores, such as deer and oxen, have an upstanding larynx and an extremely efficient food-channel, guarded above by a complete arcus; cetaceans, such as dolphins, have complete separation of air and food passages.

leads to scarring and contraction of the fauces, may itself prevent efficient removal of infected secretions by interfering with swallowing movements of the superior constrictor muscles.

Inhalation of Dust

A certain amount of filtering is attained by vibrissae at the nostrils, and still more dust is entangled in the mucoid blanket which covers the nasal mucosa, to be removed by ciliary action; the larynx is not capable of preventing entrance of small particles unless it is closed. Irritation of the mucosa may promote cough, which may momentarily expel some of the debris. Subsequently ejection of dust and bacteria depends on ciliary action in the trachea and bronchi, to be considered later.

Harmful Gases and Vapours

Since respiration can be interrupted only for a very brief period, it is obvious that poisonous gases will reach the finer bronchi in spite of cough. This is noticeable in the slight or absent damage to the larynx after exposure, while inflammation and ulceration may be produced in the bronchi. In warfare reliance has, therefore, to be placed on gas-masks.

Coal-gas may give warning by its smell, and those with anosmia are consequently in danger of asphyxiation from undetected leakages.

Winter fogs have in recent years been accused of causing widespread respiratory infections, and inhalation of sulphuric or other irritating substances cannot be excluded except momentarily, since respiration cannot be discontinued; here again, as with the gases of warfare, masks may be of use. Contaminated secretions in the bronchi rely on ciliary action for their ejection.

Protection by the Nose

Reference has been made to the warning given by the sense of smell—a warning which can do no more than cause sudden and temporary spasmodic closure of the larynx or may lead to the wearing of a gas-mask.

Certain animals—for example, newts and frogs, crocodiles, water buffaloes, and whales—can prevent entrance of water by closure of the nostrils; in man this is not possible.

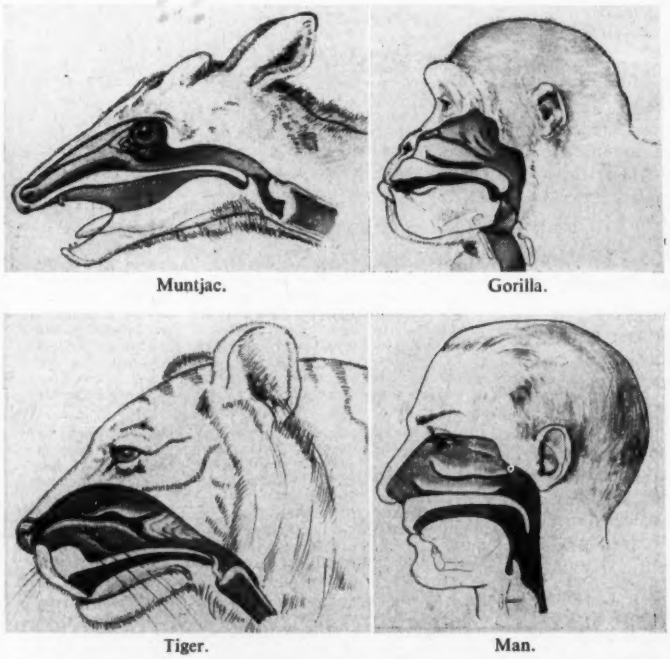
Functions of the Nasal Organ

At this stage it will be best to discuss the relationship of the nose to the lower respiratory passages; it is sometimes assumed that the main function of the nose is to help in maintaining the health of the tracheobronchial tree by arresting bacteria and dust and by warming and moistening inspired air. But when the nasal organ is examined in its primitive stages of evolution it is found to have a purely olfactory function; this is obvious in a fish such as the pike, where water entering during forward progression reaches the olfactory rosette. Various methods for drawing water over the rosette are found, some depending on the mechanism which helps to cause circulation of water through the gills; but in no instance is the nasal organ of any use in protection of the respiratory apparatus.

Lung-fish, which breathe air when the water in which they live dries up, have a communication between the nasal passage and the pharynx, but here again for the sole benefit of the olfactory sense; there is obviously no necessity for warming or moistening air.

When mammals are examined the nose is found to be divided into two sections: one anteriorly for the warming and moistening of air, and the other posteriorly for olfactory stimulation. If all mammals are examined it is found that the two sections are complementary and parallel in complexity; keen-scented animals, and especially carnivores, have a wide olfactory area and an extensive air-conditioning system, while species with feeble powers of smell, such as the higher apes and man, have a very restricted olfactory area, with corresponding reduction for warming and moistening air.

Though the lower respiratory tract benefits from passage of air through the nose, yet the nose was not designed for this purpose and does not adapt itself efficiently to alterations of climate; its primitive function is olfactory.



TEXT FIG. 3.—Relation of the palate and the larynx. In keen-scented animals such as the Indian barking deer or muntjac the epiglottis lies above the soft palate and ensures that all air shall enter and leave through the nose. Carnivora, of which the tiger is an example, have a similar arrangement, of great value when tracking prey. The gorilla relies on sight and not on scent, and no longer needs to direct all inspired air through the nose; there is a gap between the soft palate and the epiglottis. This is still more marked in man.

Air-conditioning

Respiratory exchanges of oxygen and carbon dioxide cannot continue in the alveoli unless the surface of the epithelium is moistened. The supply of moisture comes partly from the atmosphere and partly from transudation and secretion through the epithelium lining the nose, trachea, and bronchi. Air reaching the alveoli is at body temperature and is saturated with moisture; heat is essential if the air is to carry much water vapour.

In animals such as dogs, cats, and rabbits a very elaborate maxillo-turbinal body with an enormous surface, capable of alteration in area, can bring air to body temperature and to complete saturation for olfactory purposes and with incidental benefit to the respiratory tract. Man, with his degenerate sense of smell and restricted air-conditioning area, is not similarly equipped, and consequently much moisture, in addition to that from the nose, is given up in the passage of air through the trachea and bronchi (Special Plate, Fig. 1).

Knowing the importance of this function and realizing the deficiencies of the human nose, great care must be taken to preserve the nasal mucosa, limited as it is; removal of tissue from the maxillo-turbinals is highly improper. If the nose is dry from thyroid insufficiency, or rhinitis sicca or atrophica, the taking of small doses of potassium iodide is of benefit; a simple spray of sodium bicarbonate 0.5% and glycerin 10%, with chloretone 0.5% as a preservative and normal saline as a base, may be of help in encouraging production of secretion.

Air-conditioning of rooms is important, and many cases of recurrent sinusitis are caused by over-dry air; a relative humidity of 50% or even more should be attained, but is not always attained in winter.

Atmospheric air in a cold winter carries little moisture, and when warmed up in a room or hospital ward the relative humidity—which varies inversely with the temperature, falls to an unhealthy level, perhaps as low as 20%. Alternately, moist air in the summer with a high water content, when brought into a room and artificially cooled, causes the relative humidity to rise to an unpleasant degree.

Supply of Moisture by the Nose

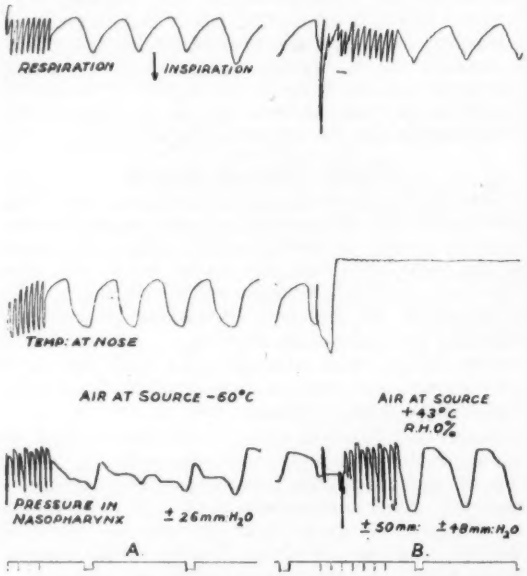
Nothing must be done to reduce the capabilities of the nasal mucosa for air-conditioning, but, on the other hand, steps may be necessary to improve matters. Of these, straightening of the nose or the septum is sometimes required, but only after estimating the relative air-flow through each nasal fossa; other forms of obstruction, as by polypi, may need attention.

Response of the Nose to Hot and Cold Climates

If the nose were directly concerned with the protection of the lower respiratory passages and lungs there would be dilatation of the arterioles and capillaries when inspired air is cold; such is not the case, since inhalation of very cold air at a temperature as low as −40° C. leads to slight vascular constriction and shrinkage of the mucosa, as shown by lowered resistance in the nose. This is similar to constriction of the skin capillaries designed to prevent loss of heat from the body. Very cold air, being dry, should theoretically lead to filling of sinusoids to provide additional moisture by transudation, but such is not the case (Text Fig. 4 A, B).

The nose retains much of the warm moisture coming from the bronchi on expiration, with advantage to the conditioning of subsequent inspirations; because of this, nasal respiration is superior to mouth-breathing, which has not the same faculty of retaining heat or moisture on expiration.

Nocturnal mouth-breathing in those whose nose is clear by day can often be prevented by the use of an oral shield placed between the lips and teeth. Bringing an obstructed nostril uppermost by turning over in bed may clear the nose by virtue of the naso-pulmonary reflex. In man there is a rising temperature gradient from the nose to the trachea and bronchi; cold, dry air reaches body temperature and saturation only when it is in the alveoli; there is a corresponding fall on expiration.



TEXT FIG. 4.—Kymographic tracings to illustrate phases of respiration (above), temperature of air entering and leaving the nose (middle), and resistance in the nose as registered by the nasopharyngeal pressure (below). A. The subject breathes air reaching the nose at about −20° C.; the temperature rises during each expiration and falls during inspiration, but is still above zero. The pressure in the nasopharynx is ±26 mm. H_2O, which is only slightly above normal. B. Hot air causes increased congestion of the nasal mucous membrane, as shown by raised pressure in the nasopharynx to a level of ±50 mm. H_2O. The air enters and leaves the nose at a level equal to body temperature.

LEGENDS TO SPECIAL PLATE

FIG. 1.—Relative size of maxillo-turbinals in man (left) and cat (right). In man the ethmo- and maxillo-turbinals are flat plates lying close to the nasal septum and with hollow unwanted spaces laterally, the maxillary sinuses; the areas for air-conditioning and for olfaction are restricted. In the cat and other keen-scented carnivores the maxillo-turbinal is widely branching, occupying the whole breadth of the snout and affording a large area for air-conditioning; the olfactory area is correspondingly extensive.

FIG. 2.—Transverse sections of cilia photographed by electron microscopy and reproduced by kind permission of Professor Fawcett. (×40,000.) Each cilium has stiffening fibrils in a protoplasmic core, nine pairs around the periphery and one pair in the centre. There is remarkable similarity between the cilia of a mollusc (A), an amphibian (B), and a mammal (C). The centre pairs of fibrils are all orientated on one axis, which is no doubt designed to ensure uniformity of bending at a right-angle to this axis, thus avoiding interference.

FIG. 3.—High-power view of part of the lamella in the olfactory recess of a carp (*Cyprinus carpio*), illustrating the large number of goblet cells secreting mucus; some cells have reached the surface and have discharged their contents. When the fish is placed in distilled water or in saline solution similar to salt water there is increased activity of the goblet cells, no doubt intended to counteract inwardly directed osmosis or outwardly directed transudation.

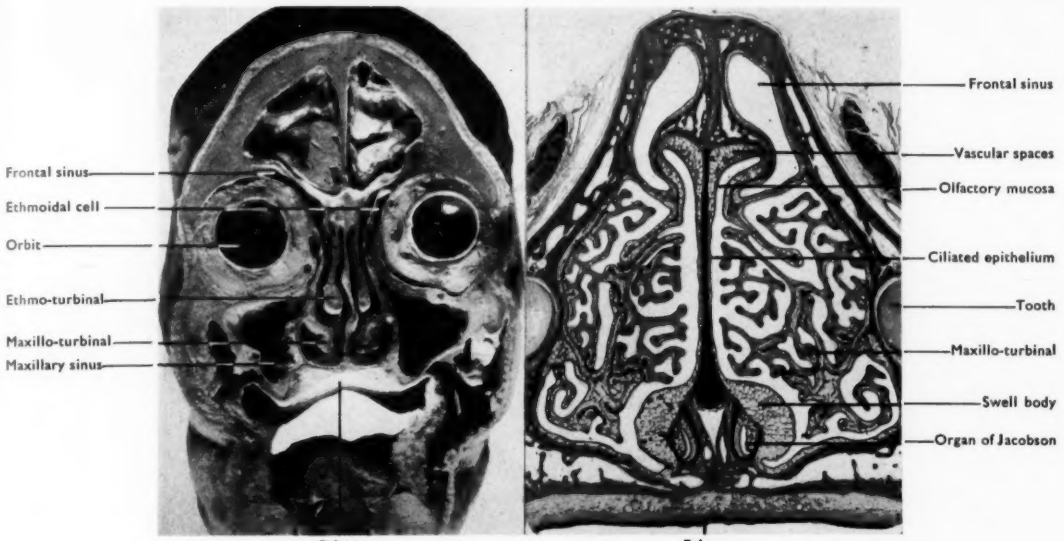


FIG. 1

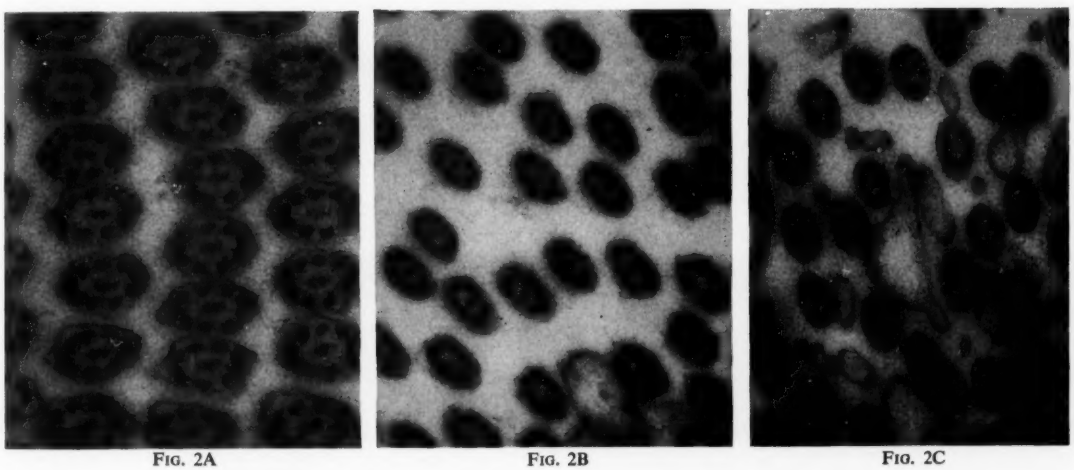


FIG. 2A FIG. 2B FIG. 2C

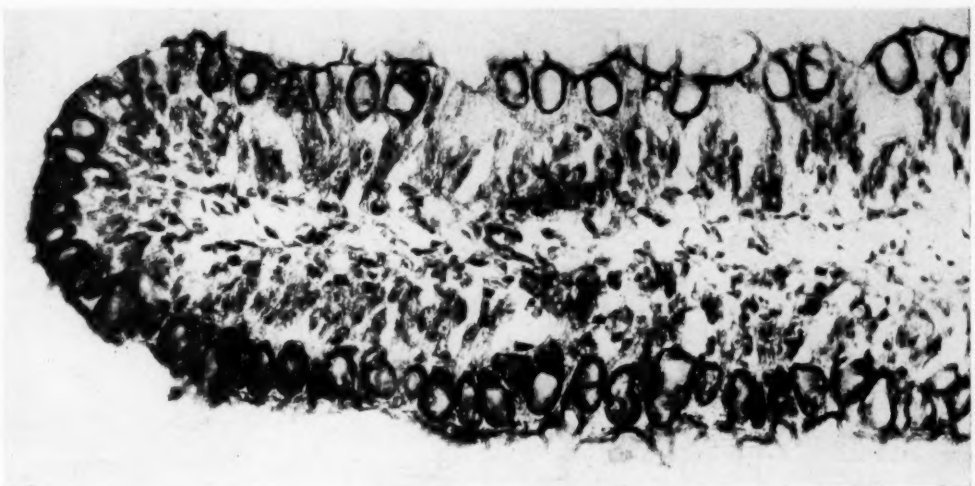


FIG. 3

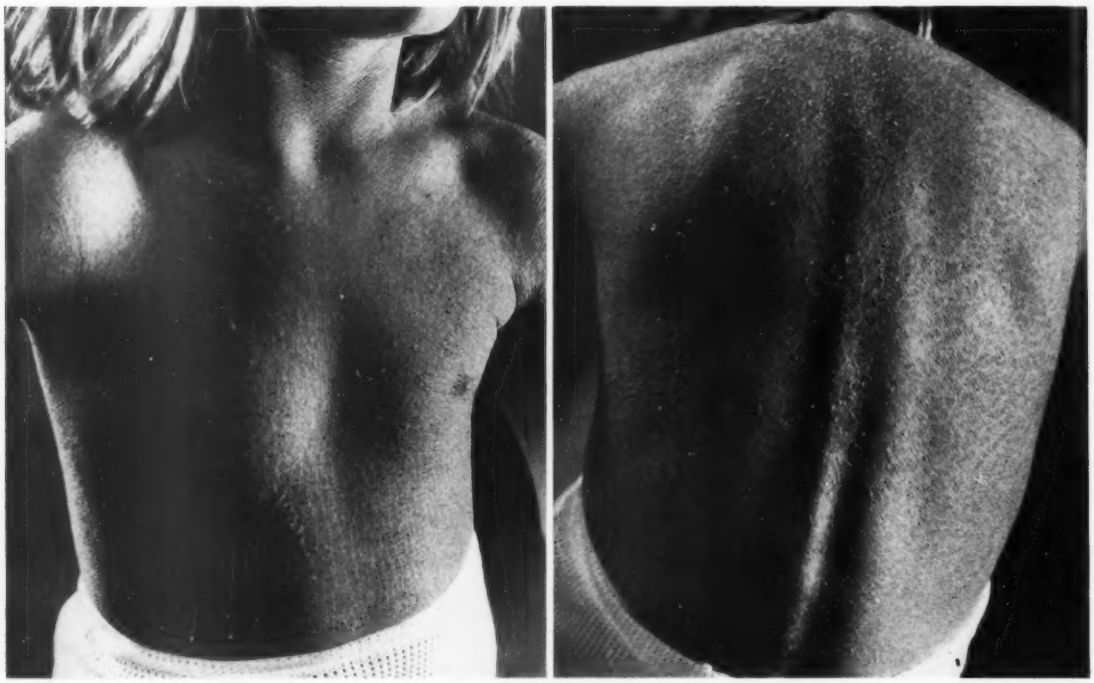


FIG. 1.—Case 1 immediately before start of treatment.

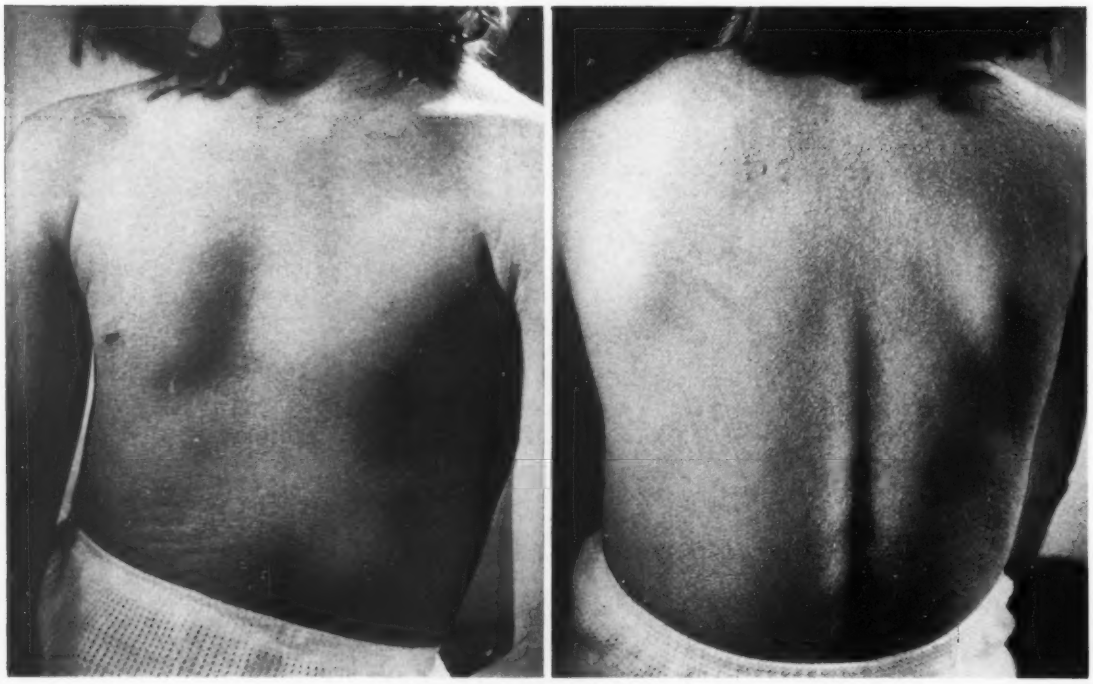
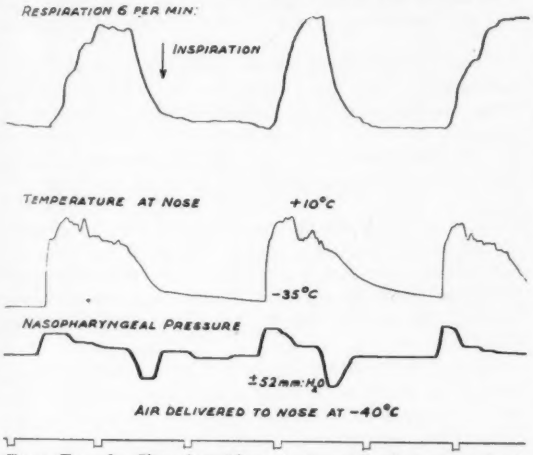


FIG. 2.—Case 1 four months after start of treatment.

Retention of heat and moisture on expiration should be remembered with the subjects of tracheostomy or laryngectomy, who should wear a shield over the tracheostome, covered with at least six layers of gauze as a partial replacement for the nose.

Hot air is reduced in temperature as it passes through the nose on inspiration; and on exertion expiration by the mouth is of advantage as a means of losing heat.

In a very cold climate mouth-breathing is highly undesirable. Very slow inspirations allow chilling of the lower air-passages, since the preliminary warming influence of expired air is much reduced (Text Fig. 5).



TEXT. FIG. 5.—Slow breathing at six respirations per minute removes most of the warming effect of expired air; the current of air reaching the nose at −40° C. falls to −35° C. at the end of inspiration. There is then a sudden rise to +10° C. at the end of expiration.

Ciliary Action

The health of the respiratory passages depends in great part on the action of ciliary streams, which are capable of expelling bacteria and small particles of dust if these happen to be entangled in the blanket of diluted mucus which overlies the epithelium. Cilia are of primitive origin and their structure is of great interest; the cilia of molluscs, amphibians, and mammals are almost indistinguishable. All have stiffening fibrils, nine pairs round the periphery and one pair in the centre; the latter are orientated on the same axis, so that waving of the cilia shall be in one direction only, with no clashing (Special Plate Fig. 2).

Cilia line the nasal fossa and sinuses, the posterior nasal passages, the trachea, bronchi, and bronchioles; there are none in the atria, air-sacs, or alveoli. Since the bronchial tree of man divides, according to Hilding, into about 50,000 branches, the task of cilia is great in cleansing these minute air-passages. Plugging of smaller bronchi or bronchioles by thick mucus may cause pulmonary collapse, requiring aspiration of the obstructing secretion.

Nothing must be done to upset ciliary action. Drastic operations on the intranasal structures, the sinuses, or posterior nasal passage may cause scarring and obliteration of ciliary streams; harm may be caused by excessive use of cauterization or ionization, or by the use of drugs with a paralysing effect, such as strong cocaine. Drying of the mucosa is fatal to ciliary action, whether by powerful vasoconstrictor drops or sprays, by prolonged inhalation of constricting vapours, by excessive doses of atropine, or by drying of the air; in this respect humidification of inspired air is important, and those with tubes in the trachea should have the surrounding air moistened to a relative humidity of at least 50% until their mucosa has become adapted to changed conditions. Even then a shield should be worn over the tracheostome.

Potassium iodide in small doses is useful in encouraging liquefaction of viscid secretions; wetting agents are sometimes required in humidified air, as in acute tracheo-bronchitis. Since the larynx cannot exclude bacteria, reliance is placed on ciliary streams and on lysozymes in the mucoid blanket. With an efficient mucoid blanket and regular removal of viruses and bacteria there should be no invasion of the epithelium; it is only when this is penetrated from lack of moisture or from stagnation by obstruction that the second line of leucocytic defence is called into action. Some who are prone to recurrent colds in the nose may be helped by vaccine treatment. In cases of acute rhinitis it is important to obviate complete obstruction of the nose by the use of steam inhalations, or, in certain instances, a spray containing 0.5% ephedrine. Entrance of foreign bodies into the bronchi leads eventually to the formation of granulations, with interruption of ciliary streams; early removal of the intruding object is essential. Infection in the form of bronchitis, bronchiectasis, or bronchial or lung abscess may necessitate removal of secretions by direct or indirect aspiration, with treatment, in certain cases, of obstructing granulations by some astringent such as protargol or silver nitrate. A growth, whether simple or malignant, will cause obstruction and infection, and so will persisting bronchospasm, as in chronic asthma.

Cough

The majority of individuals never cough and yet suffer no disability in the respiratory tract, owing to the protective action of cilia. When a foreign body tends to enter the larynx or actually passes into the trachea cough may be valuable for ejecting the intruder; but the initial deep inspiration can be a danger by drawing the object, especially if it is light, still deeper into the bronchial tree. When a foreign body is lodged in a bronchus cough may have little or no effect, because the sudden expiratory effort is accompanied by contraction of bronchial musculature, which firmly grips the object; instrumental removal is required.

Plugs of viscid secretion can often be removed by cough, but here again partial or complete muscular closure of bronchi or bronchioles tends to prevent effective clearance, particularly in asthma.

Exchange of Fluid in the Respiratory Tract

It is impossible in a short communication to discuss this subject in detail, since it is one of considerable complexity.

It is essential for the exchange of oxygen and carbon dioxide between the air in the alveoli and the blood in the pulmonary capillaries that the air should be saturated with moisture at body temperature. Water vapour is derived in varying amounts from the external atmosphere according to the degree of relative humidity; part comes from transudate and some from serous and mucoid glands and goblet cells, but there are none of these in the atria, air-sacs, or alveoli, and in consequence

the moisture for these terminal cavities enters by diffusion of air. The amount from each source depends on hydrostatic pressure, on osmosis, and on the activity of secreting cells.

To the water covering the epithelium mucin is added in varying amount, and attention must be directed to this substance. Its presence is of help to ciliary action by giving viscosity to the mucoid blanket, as Proetz has described it; but, though cohesion assists the drag of cilia from a distance, mucin is not essential for ciliary action. Cilia, in fact, work more vigorously in a watery medium, as seen in animalcules such as *Paramoecium*. But mucin, a polysaccharide insoluble in water, provides a waterproofing covering to the epithelial surface. This action may be observed in eels, whose thin and flexible skin is covered with viscid mucus. If this slimy covering is removed the fish will, if replaced in fresh or distilled water, take in so much fluid by osmosis as to swell up and die.

The lamellae in the olfactory recess of a fish such as the carp are provided with very many goblet cells, no doubt designed to waterproof the permeable olfactory epithelium (Special Plate Fig. 3).

In the respiratory tract the purpose of a mucoid blanket appears to be similar—to control outward transudation and inward osmosis through the thin and permeable epithelium, while at the same time allowing ciliary action to continue and also permitting passage of olfactory molecules.

In bronchitis excessive collection of fluid in the smaller bronchioles, probably as a result of irritating substances, interferes with respiratory exchanges; in association with this tendency to flooding there is considerable increase of goblet cells, apparently as a well-intentioned effort at protection. But increase of goblet cells entails reduction of ciliated cells, with the result that viscid secretion fills the lumen of the bronchioles and is not removed by ciliary streams.

In asthma a similar process occurs, no doubt dependent in part on increased permeability of cell membranes in an allergic state, with a coincidental rise of *p*H.

Permeability of cell membranes is influenced by the presence of calcium, a deficiency of which facilitates transudation and osmosis. Administration of calcium gluconate together with dilute hydrochloric acid may be of advantage, especially in cases of nasal allergy, in reducing oedema.

Conclusion

An attempt has been made to show how various evolutionary changes have affected the protection of the respiratory tract of man; these changes, though detrimental to the preservation of health, have been of great advantage in facilitating speech and thereby the development of man's intellect.

A plaque commemorating Dr. Marie Stopes has been unveiled at the entrance to Norbury Park Mansion, Dorking, once her home, on behalf of the Royal Society of Literature. The plaque says: "This house, built for William Lock in 1774, was for many years a favourite resort of Fanny Burney and was from 1934 to 1958 the home of Marie Stopes, scientist and author. By her it was bequeathed to the Royal Society of Literature. The society, of which she was a fellow from 1913 to 1958, has caused this plaque to be erected in her memory and in token of gratitude."

INTERFERENCE PATTERNS ENCOUNTERED WHEN USING ATTENUATED POLIOVIRUS VACCINES

BY

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An account has already been given (Hale *et al.*, 1959; Knowelden *et al.*, 1961) of a trial of Sabin live poliovirus vaccine type 2 in Singapore during the type 1 epidemic of 1958. It was shown that the number of patients who developed paralytic poliomyelitis less than eight days after vaccination was close to that expected from the rates in unvaccinated children, whereas the number of cases which occurred later was lower than the expected number. During the trial we took the opportunity of studying the interference effects between the vaccine strain and the epidemic strain and also between the vaccine strain and other existing enteroviruses.

Recently a further study of Sabin attenuated vaccine types 1, 2, and 3 took place under the auspices of the Medical Research Council. Children from Newcastle upon Tyne co-operated in this study, and we were presented with a further opportunity of observing interference effects.

SINGAPORE TRIAL

The schedules of vaccination and laboratory procedure have previously been described (Hale *et al.*, 1959).

Effect of Type 2 Vaccine Strain on Type 1 Epidemic Strain

Fig. 1 shows the days after vaccination, when clinical cases of poliomyelitis due to the type 1 virus occurred among children who had received the type 2 vaccine. Eight cases occurred within eight days of vaccination, and, as is shown later, these were in children already incubating type 1 infection when given the vaccine. There were two other cases in vaccinated children, but these cannot be included in the analysis, since vaccine was given to one who was actually paralysed and to the other after the onset of illness.

No cases occurred in children between 8 and 19 days after vaccination; it is during this period that multiplication of the vaccine strain in susceptible cells of the alimentary tract takes place and maximum interference effect would be expected. Paralytic cases that occurred later were probably instances of type 1 infection breaking through the heterologous type 2 protection acquired as a result of previous infection induced either naturally or by vaccine.

Effect of Type 1 Epidemic Strain on Type 2 Vaccine Strain

The eight cases of type 1 clinical disease that occurred within eight days of vaccination are presented in Table I.

*Now at the Department of Bacteriology, Royal Victoria Infirmary, Newcastle upon Tyne.

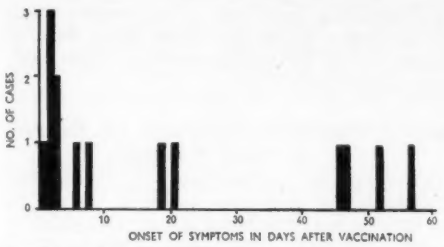
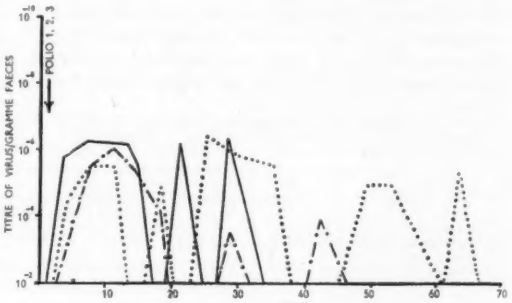
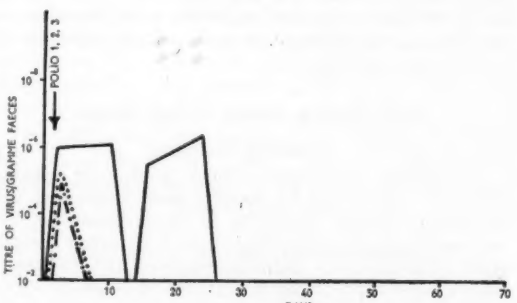


FIG. 1.—Cases of poliomyelitis occurring after type 2 Sabin vaccination. (In Figs. 2–8, · · · · · · = poliovirus 1, ——— = poliovirus 2, and — · — = poliovirus 3.)



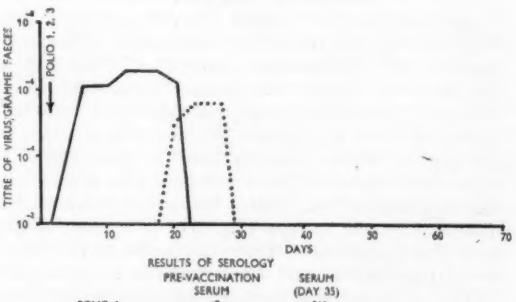
RESULTS OF SEROLOGY	PRE-VACCINATION SERUM	SERUM (DAY 54)	SERUM (DAY 183)
POLIO 1	<8	1024	256
POLIO 2	40	>512	512
POLIO 3	<8	1024	256

FIG. 2



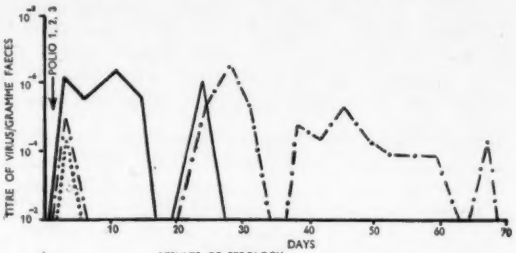
RESULTS OF SEROLOGY	PRE-VACCINATION SERUM	SERUM (DAY 36)	SERUM (DAY 182)
POLIO 1	<8	<8	<8
POLIO 2	<8	100	>2048
POLIO 3	<8	<8	<8

FIG. 3



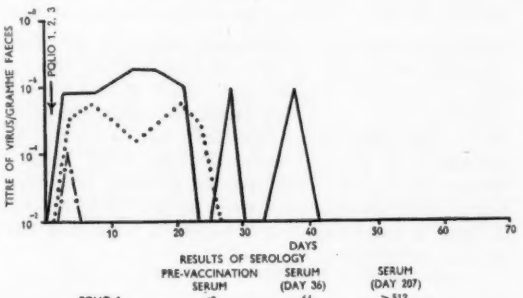
RESULTS OF SEROLOGY	PRE-VACCINATION SERUM	SERUM (DAY 35)
POLIO 1	<8	>512
POLIO 2	<8	>512
POLIO 3	<8	<8

FIG. 4



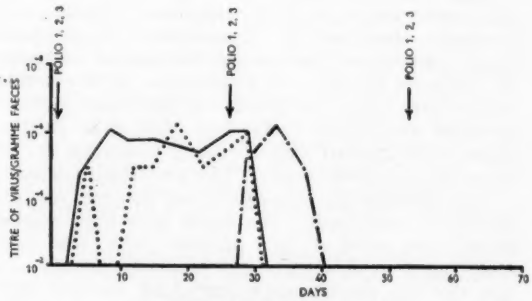
RESULTS OF SEROLOGY	PRE-VACCINATION SERUM	SERUM (DAY 35)	SERUM (DAY 183)
POLIO 1	<8	<8	<8
POLIO 2	<8	64	1024
POLIO 3	<8	64	650

FIG. 5



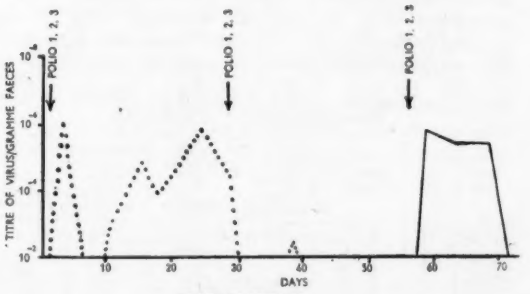
RESULTS OF SEROLOGY	PRE-VACCINATION SERUM	SERUM (DAY 36)	SERUM (DAY 207)
POLIO 1	<8	64	>512
POLIO 2	<8	26	>512
POLIO 3	<8	<8	<8

FIG. 6



RESULTS OF SEROLOGY	PRE-VACCINATION SERUM	SERUM (DAY 93)
POLIO 1	<8	>2048
POLIO 2	<8	>2048
POLIO 3	<8	256

FIG. 7



RESULTS OF SEROLOGY	PRE-VACCINATION SERUM	SERUM (DAY 91)	SERUM (DAY 253)
POLIO 1	<8	>2048	>2048
POLIO 2	<8	>2048	>2048
POLIO 3	<8	<8	<8

FIG. 8

From all but one (S.Y.T.), despite repeated attempts, we were unable to isolate the type 2 virus from the faeces. From Case S.Y.T. both types 1 and 2 virus were isolated, but the infection with type 2 was insufficient to produce antibodies, since sera obtained during the acute and convalescent stages of the disease contained antibodies to only the type 1 virus; the titres were 25 and 625 respectively. Case W.M.L. was the only one from which we failed to isolate the type 1 virus. This failure may have been due to the fact that admission to hospital occurred later after onset of illness; serological examinations showed, however, a rise of antibody to type 1 virus from 5 to 56 but none to type 2, indicating that the type 2 virus had never become established.

TABLE I.—*Poliomyelitis Cases Occurring Within Eight Days of Vaccination with Type 2 Sabin Vaccine*

Subject	Sex	Age	Interval between Vaccination and Onset (Days)	Type of Poliovirus Isolated from Faeces
S.Y.T.	M	1 year	2	1 and 2
L.Y.H.	M	2 years	2	1
C.C.	F	10 months	2	1
F.B.S.	F	22 ,,	3	1
H.B.H.	F	1 year	3	1
W.C.	F	2 years	6	1
K.K.	F	22 months	8	1
W.M.L.	F	5 ,,	1	Negative

Effect of Existing Enterovirus Infection on Type 2 Vaccination

Sabin (1959a, 1959b) has reported failure of vaccination due to persistent alimentary infection with non-polio virus strains. Examination of children's faeces immediately before the vaccination campaign in Singapore showed that a proportion were excreting enteroviruses, and a few of these children were followed up after vaccination (Table II). The three children found to be infected with a virus of Coxsackie A type responded in different ways. Two developed antibodies to type 2 poliovirus, although in one the virus was not detected in the faeces; this might have been because faeces were tested on one occasion only. The third child failed to develop type 2 antibodies, despite the fact that the faecal sample examined 15 days after vaccination was found to contain type 2 virus. In this instance, infection with Coxsackie A virus had presumably allowed only minimal growth of type 2 virus, insufficient to give an antibody response. The two children who were found to be excreting monkey-kidney-cell cytopathic agents both developed type 2 antibodies after vaccination, although type 2 was isolated from only one of them. The faeces were tested only once for virus—in this case five days after vaccination, which may have been a little early to isolate the type 2 virus. These few cases show that previous infection by an enterovirus does not necessarily result in failure of vaccination.

TABLE II.—*Response to Type 2 Vaccine of Children Excreting Enteroviruses Before Vaccination*

Subject	Sex	Age (Years)	Virus Isolated Immediately before Vaccination	Virus Isolated after Vaccination	Type 2 Antibody Titre	
					Before Vaccination	21 Days after Vaccination
C.T.W.	M	2	Coxsackie A	Poliovirus type 2	<5	<5
P.T.	M	1	,,	,,	<5	75
L.P.S.	M	2	,,	Nil	<5	25
T.A.K.	F	1	Non-polio monkey-kidney cytopathic agent	,,	<5	15
S.S.	M	4	,, ,,	Poliovirus type 2	<5	75

Effect of Vaccination Campaign on Enterovirus in the Child Population

As non-polio enteroviruses may interfere with establishment of poliovirus infection, so the converse may be expected. Table III shows the results of faecal surveys conducted in Singapore (*a*) before the vaccination, (*b*) in vaccinated children four weeks after vaccination, and (*c*) in non-vaccinated children during the campaign. As expected, the vaccinated group showed a large percentage of children infected with and excreting type 2 poliovirus. Among these children the percentage excreting other non-polio enteric viruses was significantly lower than in the group tested before the campaign began. Among the non-vaccinated children some were found to be excreting the type 1 epidemic strain and others had apparently become secondarily infected with the type 2 vaccine strain. Although not significant, the percentage excreting non-poliovirus was slightly lower in these children than in those before the vaccination campaign.

TABLE III.—*Result of Vaccination Campaign on Other Enteroviruses in the Child Population Aged 3 Months to 6 Years*

Group Tested	No. Tested	No. from Whom Virus Isolated		
		Poliovirus Type 1	Poliovirus Type 2	Non-polio Enteric Virus
Children before vaccination	229	7 (3·1%)	0	25 (10·9%)
Vaccinated children within 4 weeks after vaccination	469	0	203 (43·3%)	17 (3·6%)
Non-vaccinated children during vaccination campaign	464	22 (4·7%)	10 (2·1%)	38 (8·2%)

NEWCASTLE UPON TYNE TRIAL

Technical Methods

Vaccination Schedules.—Three groups of children aged between 6 and 12 months were vaccinated with the Sabin vaccines according to three schedules. The vaccines were given in a teaspoonful of syrup (simplex *B.P.*) Group I (13 children) received 10^6 TCD50 of each of the three types simultaneously; group II (10 children) received the same dose, but this was repeated twice more at monthly intervals; and group III (12 children) received 10^6 TCD50 of type 1, followed four weeks later by 10^6 TCD50 of type 3, and finally after a further four weeks 10^6 TCD50 of the type 2 virus.

Isolation of Virus from Faeces

After giving type 1 vaccine, in the case of children assigned to group III, a 10% suspension of faeces was made in 199 medium and spun at 10,000 r.p.m. for 30 minutes in a Spinco centrifuge. Tenfold dilutions of the supernatant fluid were made and 0.1-ml. quantities were inoculated into monkey-kidney culture tubes, two per dilution, which were incubated for seven days. The tubes were examined on the fourth and seventh days for cytopathic effects, which, when they occurred, were shown to be due to type 1 poliovirus by neutralization with type 1 antiserum. From the results of the titration of the supernatant fluid it was possible to calculate the TCD50 of poliovirus excreted per gramme of faeces.

It was not possible to use this method when dealing with faeces from groups I and II or from group III

after the type 3 vaccine had been given, as the children might be excreting two or more different virus types. Neither was it feasible to titrate the viruses in the faeces as before, then by the use of antisera ascertain which viruses were present at each dilution and so assign a titre to each. Experiments showed that in a mixture of viruses the one present in high concentration could prevent the growth of others in low concentration.

Titration of the supernatant fluids in the presence of heterologous antisera also raised difficulties, since the titres obtained were always suspiciously low. Further, it was shown that titration of the vaccine virus in the presence of the two heterologous antisera yielded titres about 4 logs lower. The antisera used were prepared in rabbits by inoculating poliovirus grown in monkey-kidney cultures, and as it seemed unlikely that the sera were non-specific, any effect was probably directly upon the tissue culture cells. Presumably the rabbit antisera also contained antibodies against monkey-kidney cells as a result of inoculation with monkey-kidney-tissue fluids. The sera were therefore adsorbed with cells from monkey-kidney cultures (300×10^6 cells per ml. antiserum) for three hours at 37° C. The vaccine strains were then titrated after neutralization against pools of the two heterologous adsorbed sera. It was then found that the titres obtained were similar to those obtained in the absence of antisera, the inhibitory substances having been adsorbed.

As a result of these findings supernatant fluids from faeces containing a mixture of polioviruses were mixed with equal quantities of pools of (*a*) types 1 and 2, (*b*) types 2 and 3, and (*c*) types 1 and 3 adsorbed antisera at 1/20 and incubated for three hours at 37° C. Tenfold dilutions were made, and 0.1-ml. quantities of each dilution were inoculated into two tubes of monkey-kidney cultures. The amount of virus per gramme of faeces was calculated as before.

The difficulty experienced has been described in some detail as it emphasizes certain dangers in the use of antisera prepared in animals by inoculation of tissue culture fluid from heterologous species.

Interference Between Vaccine Strains

Group I.—Five distinct patterns of response to vaccine were observed in the 13 children in this group. (1) Four children excreted all three types of virus over a prolonged period and produced antibodies to all three types (Fig. 2). (2) One child excreted all three types initially, but types 1 and 3 in low titre and for short duration, and showed only a type 2 antibody response (Fig. 3). (3) Three children excreted types 1 and 2, the latter dominant, but not type 3. Antibodies to types 1 and 2 were produced (Fig. 4). (4) Three children showed an initial excretion of all three types; type 1, however, was of low titre and short duration, so that only types 2 and 3 antibody responses were obtained (Fig. 5). (5) Two children showed an initial excretion of all three types with a short period of type 3 excretion in low titre and antibody responses to only types 1 and 2 (Fig. 6). It was clear that in most cases simultaneous vaccination of the three types resulted in some interference with one or more of the strains. Type 2, however, appeared to be dominant and every child developed antibodies to this type.

Group II.—As was to be expected, the same five patterns were seen after the first dose of the three types of vaccine. However, the second dose, one month after the first, allowed for colonization of the gut by strains that were interfered with at the first dose, and the example shown in Fig. 7 is typical of this group. One child who excreted all three types after the first dose, and developed antibodies to all three types, gave no response to the second dose, but after the third dose all three types were again excreted, though for a very short duration. In our experience it appears that the second dose will be sufficient to ensure that all three types become established, although a third may act as a booster in some cases.

Group III.—In general, all three types given sequentially produced infection of the gut, and antibody responses to all three types resulted. With three children, despite the absence of antibodies, one of the types failed to colonize. Fig. 8 is a typical example where the type 3 strain failed to become established in a child with no type 3 antibodies This, no doubt, was due to the type 1 virus being well established and interfering with the establishment of type 3. In the other two cases an established type 3 infection apparently prevented the type 2 strain becoming established. If sequential vaccination becomes the method of choice then the interval between doses should be extended to six to eight weeks to avoid this type of interference.

Effect of Existing Enteroviruses on Vaccination

During the trial four cases of existing enteroviruses interfering with the response to vaccination were observed.

Case 1.—A child in group II was found to be excreting an adenovirus type 1 before vaccination and for seven weeks after. Despite three doses of the mixed types, only poliovirus type 2 was recovered from the stools, and the sole antibody response was to type 2. This was the only child in the group who showed a response to one strain only.

Case 2.—A child in group I responded to the mixed vaccine and excreted all three types of poliovirus for a period of three weeks after vaccination. Coxsackie virus type B5 then appeared in the faeces, poliovirus was no longer isolated, and the Coxsackie excretion went on for a further month.

Case 3.—A child in group II excreted all three types of virus one week after the third dose. Again, Coxsackie B5 virus appeared in the faeces and all poliovirus excretion ceased.

Case 4.—As with Case 3, Coxsackie B5 virus appeared in the faeces after the third dose in a group II child and resulted in the disappearance of the three types of poliovirus present. The excretion of the Coxsackie B5 virus lasted two weeks, after which time polioviruses types 2 and 3, but not type 1, reappeared in the faeces.

In these last three cases the striking finding was the cessation of poliovirus excretion, when Coxsackie B5 virus appeared. This supplanting, however, did not cause any interference with antibody production as it occurred too late, and it probably could not have taken place earlier while the polioviruses were well established.

Discussion

There can be little doubt that enteroviruses exhibit interference patterns in natural infections in very much the same way that interference has been demonstrated in laboratory experiments (Dalldorf *et al.*, 1938; Schlesinger *et al.*, 1943; Domok, 1959). In the Singapore field trial an established infection with Sabin type 2 vaccine strain prevented subsequent infection by the type 1 epidemic strain, and this protection appeared

to be of at least 19 days' duration but probably as long as six weeks. The trial was designed to protect, but also to assess, the safety of the vaccine for both vaccinees and contacts. Since the epidemic was due to type 1 virus it would have been easy to detect cases due to type 2. In the light of our present knowledge of the safety of these vaccination procedures (Smorodintsev *et al.*, 1959 ; Chumakov *et al.*, 1959 ; Skovránek *et al.*, 1959) it would be generally agreed that now, faced with a similar incident, the vaccine of choice would be type 1.

Although interference between the enteroviruses was observed, no general pattern was evident. A prior infection might prevent the establishment of a second ; the second might be limited in such a way that no detectable antibody resulted ; or, further, the second virus might establish itself and apparently obliterate the earlier infection. In all probability the pattern that results is governed by the magnitude of the first infection, the length of time it has been present, and the magnitude of the second infection.

With attenuated poliovirus vaccine large doses such as 10^5, 10^6, or even 10^7 TCD50 are used, so that even in communities with a relatively high incidence of enteric virus infection quite good results might be obtained. Not all persons will have infection at the stage capable of interfering, and the dose of vaccine is so artificially large that it might overcome such interference. Also, in a mass campaign a child failing to become infected from the vaccine as a result of interference may become secondarily vaccinated by contact when its pre-existing enteric infection wanes.

The mass immunization with live poliovirus vaccine raises an interesting ecological possibility. It is considered that the live vaccine has a double effect: not only are antibodies produced but the intestinal tract is rendered resistant to subsequent invasion by the same type of virus. Therefore a highly immunized community might contain so few susceptibles that poliovirus circulation would probably cease. These conditions might free the field for infection with other enteric viruses, such as the E.C.H.O. group, resulting in a consequent rising incidence of conditions such as aseptic meningitis. With the disappearance of poliomyelitis, viral meningitis and encephalitis may become a much greater clinical problem.

Summary

Interference between enteric viruses was observed during the mass use of Sabin type 2 vaccine in Singapore in 1958. An established type 2 vaccine infection prevented subsequent infection with the type 1 epidemic strain for at least 19 days and probably longer. In some instances prior infection with the epidemic strain prevented colonization with the vaccine strain.

Interference effects were also observed in the trial in Newcastle upon Tyne. Administration of the three Sabin strains simultaneously as a single dose often resulted in failure of production of antibodies to types 1 or 3 and sometimes to both. Antibodies to type 2 were always produced.

An existing enteric virus infection sometimes prevented the establishment of an infection from the vaccine virus, but whether this occurred depended on the stage of the existing infection. Similarly, poliovirus circulation in a community suppressed the circulation of other enteric viruses.

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TREATMENT OF TETANUS

WITH SPECIAL REFERENCE TO TRACHEOTOMY

BY

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In the recent literature on the treatment of tetanus emphasis has been laid on intermittent positive-pressure respiration (I.P.P.R.) as the basic change in technique responsible for therapeutic improvement. But for I.P.P.R. an elaborate organization is required, and in many places neither the equipment nor the trained personnel were available. The value of tracheotomy alone has not been stressed, and the purpose of this paper is to describe the improved results that followed on the introduction of this simpler measure ; to define the indications for doing a tracheotomy, or for using I.P.P.R. ; and to outline the method of treatment which has been found most effective.

Tetanus is usually classified as severe if the incubation period is less than seven days, or if the period of invasion between the onset of the first symptom and the first generalized spasm is less than 48 hours (Cole, 1940). There are, however, exceptions to this rule, and it has been found more helpful to classify cases according to the severity of the spasms, with special reference to the effect of generalized spasms, laryngospasm, and pharyngospasm on respiratory function. Mild cases have no generalized spasms, only muscular hypertonicity. Moderate cases have generalized spasms, but these are not prolonged or frequent and do not interfere with respiration or swallowing. Severe cases have spasms that impair pulmonary ventilation in one or more of the following ways: prolonged or frequent spasms that fix the chest wall and diaphragm ; laryngospasm with complete obstruction of respiration ; and pharyngospasm which prevents the swallowing of saliva that lies pooled in the pharynx and is inhaled into the trachea. The impaired pulmonary ventilation is

manifested by anxiety, restlessness, a rising pulse rate and blood-pressure, sweating, and cyanosis. Very severe forms show signs of impending failure of the vital centres with circulatory collapse, respiratory failure, hyperpyrexia, ileus, coma, or diminished spasms with muscular flaccidity.

Any spasm severe enough to cause apnoea, which requires artificial respiration to re-establish breathing, is an important sign of impending respiratory failure, as in the pretracheotomy era a second attack of this type was invariably fatal. Occasionally severe forms are associated only with focal spasms of the larynx or pharynx (Courtois-Suffit and Giroux, 1918) which can also threaten life by obstructing respiration.

Material

Fifty-five children, excluding cases of tetanus neonatorum, were admitted to hospital with tetanus between 1951 and 1957. In many of these children the incubation period could not be accurately determined as either the history was unreliable or there were so many minor abrasions that it was impossible to decide from which site the infection arose. In 26 of them, however, the period of invasion was less than 48 hours. They were treated with intravenous and intramuscular tetanus antitoxin, penicillin, barbiturates, paraldehyde, and, in a few cases, chlorpromazine. Of these 55 children, 27 (49%) died.

Since 1958, 27 children with tetanus have been admitted to Groote Schuur Hospital and the Red Cross War Memorial Children's Hospital, of whom 14 had an invasive period of 48 hours or less. Tracheotomy was done in 14 cases and I.P.P.R. was used in four. Of the 27 children, 3 (11%) died.

Treatment

After desensitization by multiple injections of increasing strength if a routine intradermal test dose of 1 min. (0.06 ml.) of antitetanic serum was positive, all patients were given 30,000 units of antitetanic serum intravenously and 60,000 units intramuscularly. Wounds were treated solely on their surgical merits. Thickened skin was pared off and any wound examined carefully for the presence of a foreign body. Procaine penicillin was given daily for 10 days and then stopped. The sedatives used were paraldehyde and barbiturates, occasionally chlorpromazine, beginning with standard dosages and increasing until spasms were controlled. Recently mephenesin, in dosages of up to 150 mg./lb./day (330 mg./kg./day), together with phenobarbitone, has been given by stomach tube and appears to be more effective than other combinations of drugs.

Tracheotomy

Tracheotomy was done in all severe cases—that is, those with frequent or prolonged spasms; with laryngospasm; with pharyngospasm or any difficulty in swallowing; and in those showing signs of cardio-respiratory distress with a rising pulse rate, cyanosis, and sweating. It is always wiser to do the tracheotomy early rather than late, as even the first generalized spasm, especially if associated with laryngospasm, may end fatally. Much of the success of treatment depends on the technique of tracheotomy and the subsequent care of the patient. Tracheotomy is always done under general anaesthesia with an endotracheal tube passed. A very "low" tracheotomy has not been found entirely satisfactory. It requires a long tube, with an increased hazard in small children of the tube impinging on the carina. It also makes the insertion of a cuffed tube into the trachea more difficult. Furthermore, the longer the tube the greater is the likelihood that with head retraction during spasms the tip of the tube may be tilted upwards against the anterior tracheal wall, which will obstruct respiration and traumatize the trachea. It is our impression that very "low" tracheotomies are associated with a higher incidence of mediastinal emphysema and pneumothorax. There also seems to be greater difficulty when the tracheotomy tube has to be changed, and false passages are more easily made.

Initially, where size permits, a Radcliffe tracheotomy tube is inserted, because the course of tetanus is unpredictable and I.P.P.R. may be required for cases which at first appear only moderately severe. Even if I.P.P.R. is not used, the cuffed tracheotomy tube helps in preventing pharyngeal secretions from being inhaled into the lungs. The Radcliffe tube is left in for about 10 days, after which I.P.P.R. is unlikely to be required. It is then replaced by a metal tracheotomy tube. Frequent suctioning with a soft rubber catheter, obviously of small enough diameter not to impede respiration, should be started immediately after the tracheotomy as blood often runs down the trachea. Once bleeding has ceased, suctioning about every half-hour is sufficient, but it may have to be done more often if there is much secretion. It is essential that suctioning should continue until all secretions have been aspirated, but too high a suction pressure should be avoided as the tube may become attached to the tracheal wall and mucous membrane may be tugged off, causing bleeding.

Humidification must be started as soon as the patient returns from the theatre. Warm vapour is preferred to "alevaire" and must be dense enough to keep secretions loose. The need for adequate humidification cannot be too strongly emphasized, and failure to maintain adequate humidification is probably the most important cause of trouble with tracheotomies. With inadequate humidification, mucous secretions may become very tenacious and difficult to remove. When a metal tracheotomy tube is being used, the inner tube may be quite clean, but when it is reinserted sticky mucus may be scraped off the wall of the outer tube to form a plug at the tip of the tube, which obstructs respiration. For this reason tracheotomy tubes should be changed every four days. A few drops of trypsin inserted into the tube is effective in loosening inspissated mucus and blood. Free breathing should be checked, not only by auscultating the chest, but also by listening over the open end of the tracheotomy tube, where any obstruction to respiration can be heard as a wheezing sound. Even slight obstruction of the airway will increase spasms, and the inclination to increase sedation should be resisted until it is certain the air passages are clear, the tube is lying in alignment with, and not kinking, the trachea, and an *x*-ray film has excluded the possibility of the tube impinging on the carina.

The tracheotomy tube is removed only after the patient can swallow all feeds without difficulty and spasms have ceased to affect respiration. It is easier to wean a child from a tracheotomy if a small tube is inserted around which the patient can breathe, or else a tube with an opening in its upper wall which communicates with the larynx. The stoma of the tube

can then be occluded and the patient accustomed to normal breathing for some hours, after which the tube can be removed without difficulty.

Routine Care

Pulmonary infection has been most uncommon since tracheotomy allows aspiration of secretions from the trachea. Owing to the hypersalivation that seems to be a feature of severe tetanus and the pharyngospasm which prevents any swallowing, frequent suctioning of the mouth and pharynx is also necessary to limit the amount of saliva leaking into the larynx and trachea. The patient should be turned from side to back every four hours to encourage bronchial drainage. A rising pulse rate, sweating, fever, impaired air entry, and increasing spasms are far more likely to be due to mucus obstructing a bronchus and causing pulmonary collapse than to pulmonary infection. Routine antibiotic therapy is stopped after 10 days and subsequently given only if there is overt evidence of infection. Great emphasis is laid on a strict aseptic technique. Masks are worn, hands are washed before suctioning, and the rubber catheters are sterilized before being used again. Some infection tends to occur around the tracheotomy wound, but this appears to be lessened if no dressing is applied.

In all severe cases the patients were fed by a stomach tube which was passed through the nose during anaesthesia for tracheotomy. Otherwise very heavy sedation was required to overcome the spasm of the palate and pharynx, which makes passage of the tube very difficult. Extra fluids may be required as dehydration can follow a period when the patient has been unable to swallow, has sweated excessively, and has lost much saliva. Electrolyte losses in the saliva and sweat should be replaced. Milk feeds were given by stomach tube. As children are inclined to pull out the stomach tube it is necessary to restrain their arms. The stomach was aspirated before each feed in case ileus was developing, as vomiting may result in inhalation of stomach contents. Intravenous fluids were used in only two cases which developed ileus.

Traditionally, patients with tetanus are nursed in a darkened room free from noise. In adults this may be necessary, but our experience with children is that light and noise rarely provoke spasms. Tactile stimuli, however, do, and care should be taken in handling the child. Frequent suctioning of the mouth and trachea at short intervals may be preferable to prolonged suctioning as this is a potent cause of spasms. One child was of interest in that whenever he had a severe spasm of the neck he would cry out to the nurse to bend his head forward, which relieved the spasm. This suggests that spasms are to some extent self-perpetuating and that hyperextension of the neck and trunk should be prevented so far as is possible. While the patient is turned on his side pillows are used to keep the head forward as much as possible and to prevent excessive opisthotonos.

Fever seems to be part of the clinical picture of severe tetanus, but a rise in temperature may also be due to inadequate ventilation, dehydration, or infection. Active steps are taken to lower the temperature if it rises above 102° F. (38.9° C.). The patient is stripped and exposed, and if that does not lower the temperature a fan is made to blow on the body. Urinary retention is fairly common and may require catheterization. Constipation is the rule in severe cases, but while the child is on milk feeds no active steps are taken unless ileus develops, when intravenous fluids are given and gastric aspiration is carried out. Nurses should be told to report at once any change of condition, rise in pulse rate, sweating, or cyanosis, but this does not alter the fact that the outcome of this disease is largely determined by the frequency with which the medical staff check on the state of the patient.

Intermittent Positive-pressure Respiration

All cases are given a trial of sedation and tracheotomy, and only if this treatment fails, as judged by the occurrence of one of the following criteria, is I.P.P.R. started. (1) Spasms of such severity as to interfere with respiration and which cannot be controlled by sedation, or which require such heavy sedation as to depress respiration. (2) Respiratory failure due either to heavy sedation, or to brain-stem intoxication, or to cerebral anoxia, or to a combination of these factors. Respiratory failure may also be due to an overwhelming toxaemia causing a flaccid weakness of muscles. (3) Hyperpyrexia of over 104° F. (40° C.). (4) Increasing cardio-respiratory distress with a rising pulse rate, sweating, and cyanosis which, if allowed to persist, will go on to collapse.

The care of the patient on I.P.P.R. has been covered by a number of authors (Lassen *et al.*, 1954; Smith *et al.*, 1956), and it is only necessary to comment on a few minor points of difference. Generally, weaning from the pump was attempted at an earlier time than is customary. It is felt that the hazard of some mechanical or therapeutic failure is great enough while the patient is curarized and on I.P.P.R., and that attempts should be made to wean from about the tenth day. Spontaneous breathing is preferred even though the spasms are not yet fully abated. While the child is curarized no sedation is used as it is our impression that in most severe cases the patients are not conscious. None of the children had any recollection of what had occurred. All of them showed signs of recovering consciousness, however, before it was possible to stop I.P.P.R.

Recently a change in technique has been found which is effective in clearing the bronchi of secretions. The child is disconnected from the respirator and ventilated with an anaesthetic handbag. The chest is then alternately forcefully inflated and manually compressed in a cough-like manner. Secretions are brought up into the main bronchi and trachea, from where they can be sucked out with a catheter. A similar manœuvre while on the respirator seems only to increase the amount of pulmonary collapse. This suggests that the essential change is overinflation of the lungs, just as in a cough, which may dilate the bronchi, loosen secretions, and allow air to get behind the obstruction from whence, with a forced expiration, secretions are dislodged into the large bronchi.

The following case record is included to show the natural history of a severe case of tetanus treated with tracheotomy and sedation.

A boy aged 6 years was admitted to hospital on December 28, 1959. Fourteen days previously he had trodden on a rusty nail. For four days he had complained of pain in the back, abdomen, and jaw, and it was noticed that he had trismus. For 24 hours generalized spasms had increased in severity and frequency until they were occurring

about every one to five minutes, and on two occasions had been associated with cyanosis. The child had been unable to swallow because of a feeling of a lump in the throat. On examination his temperature was 104° F. (40° C.), pulse 160–170, and respirations 40. He was a conscious, co-operative boy with frequent generalized tetanic spasms lasting up to four minutes and causing cyanosis. Tracheotomy was done under general anaesthesia and a Radcliffe tracheotomy tube inserted. Phenobarbitone 65 mg. was given six-hourly and elixir of mephenesin 240 mg. hourly by stomach tube. Over the next two days these were increased to phenobarbitone 65 mg. four-hourly and mephenesin 360 mg. hourly. For the first week the temperature fluctuated between 100 and 103° F. (37.8 and 39.4° C.). On the third day the pulse fell to 130. Thereafter, on the eighth day the spasms were less severe; twelfth day, the amount of saliva suctioned from the mouth was lessening; fourteenth day, he was able to nod in assent, and saliva no longer exuded from the lips during a spasm; sixteenth day, mephenesin was reduced; eighteenth day, mephenesin was stopped. On the twentieth day the temperature finally settled and the stomach tube was removed. The tracheotomy tube was removed on the twenty-third day. At this stage phenobarbitone was reduced to 32 mg. six-hourly and was finally stopped after five weeks. He was discharged home after six weeks, having been given his first prophylactic injection of tetanus toxoid.

Tetanus does not confer active immunity and all cases on recovery should be actively immunized with tetanus toxoid.

Deaths

In the three children in our series who died the cause of death was quite clear. In one the tracheotomy tube appeared to be lying badly in the trachea from the onset. There was undue hesitancy about changing the tube as early as the day after operation, and when it was finally decided to do so the child died as the E.N.T. surgeon arrived. The second death was due to an occlusive tracheobronchitis. The third child died because a connexion worked loose on the fourteenth day just when he appeared to be recovering from very severe tetanus which had to be treated with I.P.P.R.

Discussion

In 1836 Thomas Curling first suggested that tracheotomy might help in the treatment of tetanus, although he never actually treated a case. The first recorded use of tracheotomy was by Humphry (1856); the patient, however, died.

Routine tracheotomy for severe cases was started about 10 years ago. Creech *et al.* (1950), having at first strongly recommended its use, subsequently (Creech *et al.*, 1957) were prepared to concede only a reduction of 10% in the mortality and thought that some of the decrease in mortality was simply a continuation in a trend that began 50 years ago. Adriani and Kerr (1955) were inclined to give credit to tracheotomy as having contributed most to the reduction in mortality (100 cases with 32 deaths). Both their mortality rates, nevertheless, are lower than in most reported series in which tracheotomy was not part of the routine therapy. Curling (1836) records a death rate of 54% of 128 cases; Johnstone (1958) 56% of 100 cases; Adams (1958) 44% of 100 cases; and Brown *et al.* (1960) 49% of 41 cases. Only Veronesi (1956), with the remarkable mortality of 18.2% of 236 cases, has achieved a low mortality without tracheotomy. In Capetown, Slome (1953) found a mortality of 43% in 137 cases treated between 1947 and 1952. The mortality of 49% in 55 cases in our series is in keeping with most other series without tracheotomy. In our opinion there has been little doubt that the dramatic fall in the mortality has followed upon the introduction of tracheotomy for severe cases. Even if the three survivors who were treated with I.P.P.R. are included in the failures the mortality is still only half that of the earlier series.

Tracheotomy, especially in small children, has the reputation of being a somewhat hazardous procedure. Undesirable results are likely to occur when it is done either too late or as an emergency under local anaesthesia and the operation has to be hurried because of respiratory obstruction. Then excessive bleeding, cerebral anoxia, and complications like mediastinal emphysema and pneumothorax are more likely to occur. When an elective tracheotomy is done under general anaesthesia with an endotracheal tube passed, it has been found a safe procedure at any age. Most trouble arises during the subsequent care and nursing because of inadequate humidification and suctioning, and from failure to observe any obstruction of the airway. It is noticeable that trouble rarely occurs with the tracheotomy tube while the patient is on I.P.P.R., presumably because the machine maintains good humidification.

There can be little doubt that tracheotomy is as rational a procedure for tetanus as it is for severe laryngeal obstruction and for head injury with coma where the patient cannot swallow his saliva. Furthermore, the effect on respiration of severe tetanus is much the same as in severe poliomyelitis with pharyngeal, laryngeal, intercostal, and diaphragmatic involvement except that the one is a spastic and the other a flaccid palsy. The main purpose of tracheotomy is to prevent the anoxia and hypercapnia associated with laryngospasm and retained pharyngeal secretions, and, by lessening the dead space, to make more effective breathing that is restricted by intercostal and diaphragmatic spasm. Anoxia potentiates tetanic spasms which demand heavier sedation until respiration is depressed with further increase in anoxia. Tracheotomy breaks this vicious circle. The effectiveness of tracheotomy in relieving anoxia and infection comes as no surprise when the amount of secretion aspirated from the trachea is seen at operation. The subsequent fall in the pulse rate, the reduction in the amount of sedative required to control spasms, the lessening of cyanotic attacks, and the rarity of pulmonary infection all testify to the effectiveness of the procedure. Furthermore, sudden death following on laryngospasm has not been seen since routine tracheotomy has been done.

Tetanus occurs most often in the underdeveloped areas of the world, where facilities for I.P.P.R. may not be available. Most hospitals, however, can deal with a tracheotomy, and if nursing facilities are limited the remarkable example of Adriani and Kerr (1955) can be quoted where "a member of the family is taught to suction secretions from the pharynx and trachea." If I.P.P.R. is available we still prefer a trial with tracheotomy and sedation, and resort to I.P.P.R. only when the indications are that this is likely to fail. While there should be no hesitation in instituting I.P.P.R. when it is required, it should be stressed that it is a worrying procedure by no means devoid of risk, particularly if nurses and resident staff are constantly being changed.

One other factor that may have played a part in the improved results in this series is the use of mephenesin as a relaxant. When combined with a barbiturate, it has

been found by Adriani and Kerr (1955) to be the most effective drug. First used in neonates, we have used it with success in the last seven older children. In three children treated with paraldehyde, phenobarbitone, and tracheotomy who were having such severe spasms that I.P.P.R. was contemplated, a change from paraldehyde to mephenesin resulted in satisfactory control. In adults it has been used intravenously rather than by mouth, but in children it has proved effective when given by stomach tube. Because of its local anaesthetic action this is preferable to oral administration, which may lead to depression of pharyngeal protective reflexes. It has shown none of the recognized complications of fall in blood-pressure, haemoglobinuria, or thrombophlebitis.

It cannot be too strongly stressed that tetanus is a preventable disease and that active immunization with tetanus toxoid is a safe procedure that should be carried out in all communities. The use of antitetanic serum in prophylaxis is far less satisfactory as it carries a considerable hazard from serum reactions. It has also been shown recently to be ineffective if the recipient has had horse serum or has an anaphylactic reaction (Godfrey *et al.*, 1960). Furthermore, severe and fatal tetanus can follow upon the most trivial injury for which the patient is unlikely to receive any prophylactic antitetanic serum.

Summary

In a series of 55 children with tetanus in which routine tracheotomy was not done, 27 (49%) died, while in a comparable group of 27 children in which tracheotomy was done in 14 severe cases and I.P.P.R. was used in 4, there were 3 deaths (11%). Apart from the use of mephenesin in some of the latter group, treatment was essentially the same.

Reasons are given why tracheotomy should be part of the routine treatment of severe tetanus.

The indications for and the technique and subsequent care of the tracheotomy in patients with tetanus are described.

Even if I.P.P.R. is available, it is felt that tracheotomy and sedation should be tried first, and only if this treatment fails, as judged by certain criteria, should I.P.P.R. be applied.

We thank Professor F. J. Ford for facilities, and Dr. D. V. Maytham, who did most of the tracheotomies. We are also grateful to Dr. J. Burger, medical superintendent of Groote Schuur Hospital, and Dr. J. F. W. Mostert, of the Red Cross War Memorial Children's Hospital, for permission to publish.

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AN INVESTIGATION OF SELECTIVE DEAFNESS PRODUCED BY DIRECT SUGGESTION UNDER HYPNOSIS

BY

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Many aspects of psychogenic deafness as encountered clinically in association with psychopathology have already been demonstrated in deafness produced in normal persons by direct suggestion under hypnosis (Erickson, 1938; Pattie, 1950). Such work to date has dealt only with deafness extending over the whole aural spectrum (total deafness). We have reported, in a preliminary communication, on the production of frequency selective deafness in this way (Black and Wigan, 1960), and we have now carried out further interpretation of our data and have performed a number of additional experiments.

Some of Erickson's subjects, in whom he produced various degrees of such total deafness by direct suggestion under hypnosis (D.S.U.H.), claimed to have subjective experiences of selective deafness, or were said to relieve anxiety by retention of the hearing of a single sound, such as the ticking of a clock. There was also objective evidence in some subjects of other sensory and even motor disturbance associated with this deafness: dilatation of the pupils, focusing disturbances, and nystagmus. One subject experienced concurrent general anaesthesia, with the greatest loss in arms and legs.

Pattie investigated unilateral total deafness produced by D.S.U.H. Earlier, Dynes (1932) experimented on the selective hearing produced by hypnosis *per se*, using the sound of a pistol-shot as the stimulus. Records were made of respiration, heart rate, and the psychogalvanic reflex (electrical resistance of the skin) both in the waking state and under hypnosis. Startle responses were reported to be absent under hypnosis, and no effect was observed on the heart rate or respiration. Slight changes of the electrical resistance of the skin were recorded. Total deafness can also be produced by post-hypnotic suggestion. This was investigated by Lundholm (1928), who showed that conditioned reflexes could not be established after such suggestions of deafness had been made and a sound tick was used as the conditioned stimulus and an electric shock as reinforcement.

Method

In our experiments records were made of the auditory thresholds of six deep-trance hypnotic subjects, first in the waking state and again after selective deafness to tones of specific frequency had been suggested under hypnosis. The evidence of deafness was then further investigated clinically and with the aid of positive conditioned reflexes, using an electric shock as the conditioning stimulus (reinforcement), tone as the conditioned stimulus, and heart rate as the conditioned response.

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In measuring the auditory thresholds of our subjects we were not concerned with any of the manifestations of clinical deafness as defined in terms of an accepted norm of auditory acuity according to British or American standards, since we were interested only in the investigation of temporary changes as these might be produced in the normal threshold of each subject as recorded in the circumstances of the experiment. The subject lay on a couch and wore high-fidelity headphones (Permoflux ; P.D.R.-10) fitted with soft rubber ear-pads to minimize ambient noise in the laboratory, which was estimated at 30/40 phons. The test-tones were thus presented binaurally and the auditory thresholds were measured between 100 and 10,000 c/s. Two methods were used for presenting the test-tones in the headphones.

In Method I tones of variable but precisely known pitch were produced by the operator by means of a hand-operated pulse generator in circuit with a Muirhead–Wigan decade audio-oscillator (part of a T.M.S. tester No. 1, Mk. II). By use of a variable octave filter, any distortion due to the oscillator was kept to less than 0.1%. In this method the intensity of the tone was controlled by the operator, and the various tones from 100 to 10,000 c/s were presented at random in groups of one, two, or three pulses. Each pulse had a smooth rise and fall, with a width of 50 msec. measured at half-height. The subject flashed a signal-light in accordance with the number of pulses heard. To establish as rapidly as possible a close approximation to the hearing threshold, pulses were first presented at the maximum level available (+100 dB ref: 0.0002 dyn/cm.^{2}), and then lowered, at first in large steps and later in smaller steps, it being taken that the threshold had been approximated when, on making a further 4 dB drop in level, either there was no response at all or the number of signal-flashes could no longer be correlated with the pulses.

In Method II a Békésy audiometer (made from a modified Marconi acuity meter: T.S. 444A) provided a gliding tone, the frequency rising throughout the test at the rate of about half an octave per minute, the total period of any one test lasting a little more than 15 minutes. In this method a spring switch operated by the subject either decreased the intensity of the tone when depressed or increased it when released. The intensity was thus controlled by the subject and the result was recorded automatically in ink on paper.

No subject was accepted for the experiment if there was any history or complaint of defective hearing, and the auditory threshold, according to the experimental technique involved, was recorded first in the waking state. Every subject was also tested after each experiment to ensure that the hearing threshold had effectively been restored to normal in terms of the ante-hypnotic value. In this respect specific checks were made at the frequency of the tone to which deafness had been suggested and at all other frequencies where changes in the threshold as recorded had been or might have been observed.

After making the preliminary record of the subject's normal threshold under these circumstances, the subject was then hypnotized and the specific frequency involved was presented for three seconds as interrupted tone in the headphones, solely for purposes of preliminary identification. Suggestions were then made that after a count down from 20 to 1 the subject would be deaf to this tone only and to nothing else. Records were taken of the actual words used in making these suggestions, and at the outset the words "you will not hear this *note*" or "you will not hear this *sound*" were arbitrarily employed. In all cases the specific frequency selected was next presented as constant tone at an intensity level of 80 dB sound pressure level (S.P.L.) over a period of 20 seconds. The count down from 20 to 1 was made during this 20-second period. As a preliminary and entirely subjective test for the suggested deafness the subject was then presented with tone as a series of pulses, only some of which were of the specific frequency involved. Failure to report on these was taken as evidence on which it was reasonable to proceed further with the experiment. The auditory thresholds of the subjects were then measured by one or other, or both, of the two methods described, and the deafness present was also investigated by other means.

In two cases positive conditioned reflexes were established beforehand. The subject attended daily at the same time for eight days and was presented alternately with tone of 310 c/s and 130 c/s for five-second periods, at one-minute intervals, during one hour. The hearing of the higher tone of 310 c/s was constantly reinforced during the first 0.05 second of the fourth second with an electric shock, produced by a short transient condenser-discharge (time constant = 50 msec. ; peak current 4 mA). Evidence of a conditioned response in the heart rate was looked for on the ninth day.

The apparatus consisted of a two-channel cathode-ray-tube assembly, one channel of which displayed changes in cardiac potential, using only the standard E.C.G. lead II (right arm, left leg). The electrodes through which the electric shock was given to the subject during conditioning were attached to the left hand. The second channel displayed a one-second time trace as well as the time and duration of the conditioning stimulus. The results were recorded by a cine camera on film, both tubes being photographed at once.

In early experiments cardiac period was measured from R to R wave, using a photographic enlarger and working from the second scale on the film. But this was found to be inaccurate as well as laborious, and in later experiments the associated amplifier was rearranged so that the deflection of the trace was proportional to the cardiac period between any two heart beats.

Conditioned-reflex Experiments

Three conditioned-reflex experiments in all were performed on the two subjects chosen for this part of the work. In C.R. Experiment I (Subject 6) records were made of the conditioned reflex 48 hours before the experiment, 10 minutes before, during the experiment, and 10 minutes afterwards. During the experiment the subject was hypnotized and presented initially with the tone of 310 c/s, to which he had been conditioned, and a record was made of the cardiac response. Deafness to the tone of 310 c/s was then suggested according to the standardized technique. The tone was again presented and four records were taken. Still under hypnosis, the subject was then cleared of all previous suggestions and, with normal hearing restored, a further record was obtained. Finally the subject was woken up and after an interval of five minutes another record was taken.

In C.R. Experiment II (Subject 1) evidence of the established conditioned reflex was obtained 24 hours

before, half an hour before, and 45 minutes after the experiment, which was otherwise identical.

In C.R. Experiment III (Subject 1) evidence of the established conditioned reflex was obtained 24 hours before, 10 minutes before, and 50 minutes afterwards. In the course of this experiment, post-hypnotic suggestions of selective deafness were also made and an independent witness was called in to examine the subject clinically while she was in the waking state but still showing evidence of being deaf to the conditioned stimulus—namely, tone of 310 c/s.

Throughout these conditioned-reflex experiments records with the cine camera were made during one minute before and for one minute after the conditioned stimulus, in order to provide ample material from which to analyse the results. In calculating the true deviation attributable to the response, both the general trend of the heart rate and the mean of the normal variation under the conditions of the experiment were taken into account.

Results

These results may be divided into three groups: (*a*) the evidence of selective deafness produced by D.S.U.H.; (*b*) the apparent significance of the words used, or the semantics involved, when making the suggestions of selective deafness to the hypnotized subjects; and (*c*) the results of the conditioned-reflex experiments aimed at further objective confirmation of the selective deafness.

Evidence of Selective Deafness

It was found that the hearing of tones at the specific frequencies tested (F_0) between 250 and 1,000 c/s and at a maximum intensity of 100 dB S.P.L. (the maximum considered safe for the subjects at the duration used) could be inhibited by D.S.U.H. It was found that in some subjects this inhibition tended to decay after periods varying from 10 to 30 minutes, while in others inhibition remained until removed by counter suggestion. In those subjects giving evidence of short-term decay, certain records made with the Békésy audiometer had to be abandoned when the period of inhibition was less than 15 minutes—the time required for the machine to sweep from 100 to 10,000 c/s.

Fig. 1 shows the change in the auditory threshold of a hypnotized subject to whom deafness to tone of 575 c/s (F_0) had been suggested under hypnosis, as recorded by Method I. It expresses, therefore, the difference between the waking-state threshold under the conditions of the experiment and that produced by D.S.U.H. Fig. 2 shows a similar result as obtained in an experiment with the Békésy audiometer (Method II). Here the change of threshold followed D.S.U.H. of deafness to tone of 500 c/s. To derive this curve, each Békésy tracing was rendered first as a line joining the mean points of the successive excursions of the recording pen in the y axis—characteristic of this instrument—and the difference between these two curves was then plotted. Fig. 3 shows the actual Békésy record of the experimental result in this case, superimposed on the preliminary control tracing of the normal ante-hypnotic threshold, rendered here as a dotted line.

On examination of the subjects when selectively deaf in this way, no response to startle situations created with tone at F_0 was elicited. There was also no evidence of voice-raising in the presence of continuous loud tone at F_0 presented at the maximum intensity permissible, and voice-lowering did not occur on cessation of loud tone at F_0. Examination with tuning-forks showed that hearing by bone conduction was also inhibited at F_0 or frequencies near to F_0, and there was thus no response to the Rinne or Weber tests. Unfortunately, tuning-forks vibrating at the precise frequencies of the various values of F_0 selected were not always available.

In some subjects it was noted that hearing by bone conduction was also inhibited at frequencies far from F_0, although hearing by air conduction at these other frequencies was present. Peripheral vibratory sense was also absent in all subjects at F_0 or frequencies near and in some subjects at all frequencies tested.

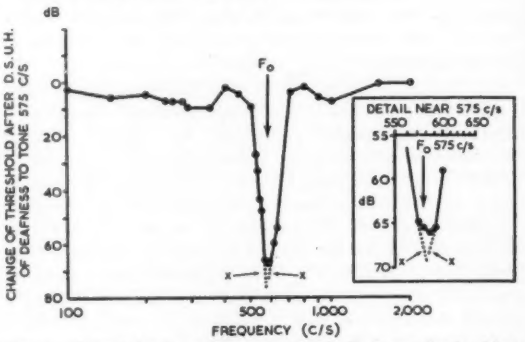

FIG. 1.—Change in the auditory threshold of a hypnotized subject. (Method I.)

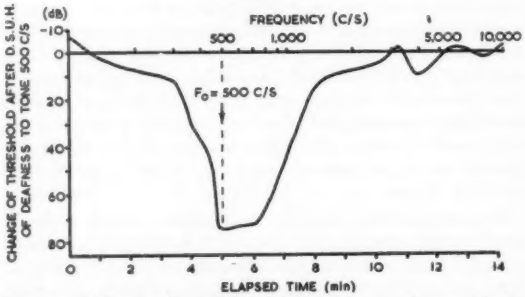

FIG. 2.—Similar result as Fig. 1, obtained in experiment with the Békésy audiometer. (Method II.)

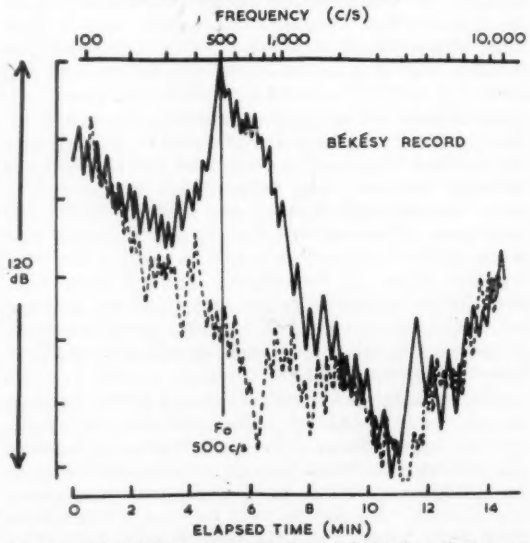

FIG. 3.—Actual Békésy record of the experimental results in same case as Fig. 2.

Apparent Significance of Words Used

It became evident that in certain subjects this selective deafness at F_0 sometimes included not only the test frequency but also half ($\frac{1}{2}$ F_0), occasionally twice this frequency (2 F_0), and in the case of one subject a third of this frequency ($\frac{1}{3}$ F_0) (Fig. 4: Method I). Examination of the suggestions made as recorded, then indicated that these discrepancies might be due to inadvertent variations in the actual words used prior to the count down. In particular there appeared to be a distinction between the effect of the words "you will not hear this note" and "you will not hear this sound."

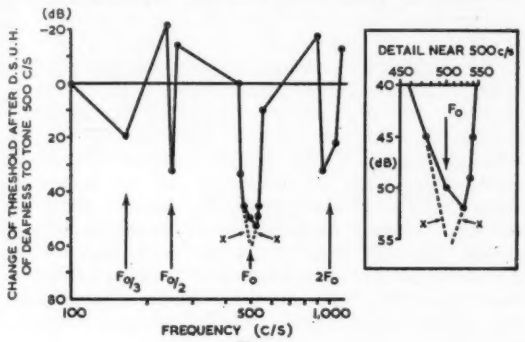

FIG. 4

This was investigated further, and it then became apparent that some such relationship did exist. All subjects were deaf to F_0 whatever the words used. But in experiments with five subjects out of six there was a predominance of inhibition of deafness to F_0 alone when this was described as a "note." When, however, F_0 was described to three of these five subjects as a "sound" they tended to include deafness to $\frac{1}{2}$ F_0. In one subject, a Welsh medical student with a good singing voice and an "ear for music," the distinction as between "note" and "sound" was reversed: in his case deafness to F_0 suggested with the words "you will not hear this sound" produced only a single trough at F_0 in the auditory threshold record. The words "you will not hear this note," however, produced troughs at $\frac{1}{2}$ F_0 and 2 F_0 as well. In one experiment (Fig. 4) he also became deaf to $\frac{1}{3}$ F_0.

Questioned in the waking state about the sort of distinction they might make between the words "note" and "sound," none of the six subjects provided an answer which could be related to the observed phenomena. Questioned under hypnosis, however, all six were able to make an immediate and significant distinction. The subjects giving predominantly F_0 only to the word "note" said, in effect, that to them a note was a single pure musical experience, and that therefore it included nothing but the single tone presented in the headphones. The one subject giving $\frac{1}{2}$ F_0, F_0, and 2 F_0 to the word "note" (and F_0 only for "sound") stated under hypnosis that, in effect, to him the word "note" also had a musical connotation, but that in music he always expected to hear harmonics whenever he heard a note. "I have never heard middle C on the piano without hearing it reflected in at least the C above and the C below," he said.

The accompanying Table gives a record of the results as the selective deafness could be related to the semantics involved in the course of making the suggestions during the different experiments.

Results of Conditioned-reflex Experiments

The two subjects (Nos. 1 and 6) selected for the conditioned-reflex experiments were one giving predominantly F_0 alone to the word "note" and the one giving F_0 alone to the word "sound" respectively, and these words were appropriately employed to give the F_0 response only. Satisfactory conditioned reflexes were established in both subjects to tone of 310 c/s, so that they showed a significant increase in heart rate (decrease in cardiac period as measured) when presented with this tone unreinforced. There was no evidence of a response to tone of 130 c/s in either subject.

The average results of four tests with Subject 6 (C.R. Experiment I) are shown in Fig. 5. A more effective and simple way of revealing any significance in the heart-rate data recorded, however, is to superimpose a number of groups of data as in Fig. 6—C.R. Experiments II and III. In curve A two sets of data from the two experiments have been averaged and the increase in heart-rate (the conditioned response) associated with the conditioned stimulus (tone of 310 c/s) is clearly demonstrated. In curve B six sets of data have been averaged from the records made in both experiments when the subject was hypnotized and direct suggestion had been given with the words "you will not hear this

TABLE I

Subject	Method of Presentation of Tone	Semantics: "You will not hear this *note*" $\frac{1}{2}$ F_0	F_0	2 F_0	Semantics: "You will not hear this *sound*" $\frac{1}{2}$ F_0	F_0	2 F_0
1 F	Pulses I	−	+	−	+	+	+
					+	+	−
					+	+	+
	Békésy II	−	+	−	+	+	−
		−	+	−			
2 F	Pulses I	−	+	−	+	+	•
		−	+	−	+	+	−†
		−	+	−	+	−	−†
	Békésy II	−	+	−	+	+	−
		+	−	−†	+	+	−†
		+	+	−	+	−	−†
3 F	Pulses I	+	−	−†	Not tested		
		−	+	−			
	Békésy II	−	+	−	,,	,,	
4 F	Békésy II only	−	+	−	,,	,,	
		−	+	•			
		−	+				
5 M	Pulses I only	Not tested			+	+	•
					+	+	−†
					•	+	+
					+	+	•
6 M	Pulses I	+	+	+	−	+	−
	Békésy II	+1/3 F*			−	+	−
		+	+	+			

* Test did not include this frequency.
† Decay of inhibition prior to completion of test.

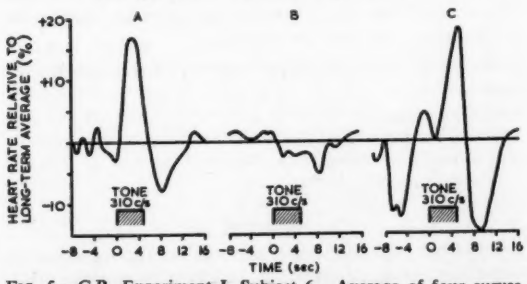

FIG. 5.—C.R. Experiment I, Subject 6. Average of four curves. A, Conditioned response. B, Response after D.S.U.H. of deafness to tone 310 c/s. C, Response after clearing suggestions of selective deafness.

note" (Subject 1). The result clearly fails to reveal any trace of the conditioned response pattern shown in curve A. None of the six individual curves, of which curve B is the average, indicated the presence of the conditioned response, and it was decided that no further analysis of a statistical nature was necessary to reinforce this evidence. This response, as in curve B, was throughout remarkably similar to the responses recorded when the subject was presented with tone of 130 c/s—to which, of course, no conditioned reflex had been established.

During C.R. Experiment III, suggestions of post-hypnotic deafness to F_0 were made after the records

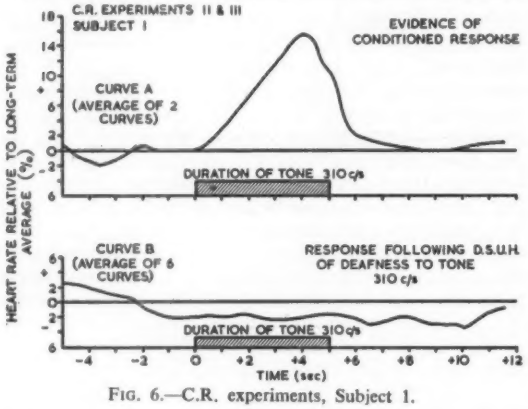
C.R. EXPERIMENTS II & III
SUBJECT 1
EVIDENCE OF CONDITIONED RESPONSE
CURVE A (AVERAGE OF 2 CURVES)
DURATION OF TONE 310 c/s
CURVE B (AVERAGE OF 6 CURVES)
RESPONSE FOLLOWING D.S.U.H. OF DEAFNESS TO TONE 310 c/s
DURATION OF TONE 310 c/s
HEART RATE RELATIVE TO LONG-TERM AVERAGE (%)
TIME (sec)

FIG. 6.—C.R. experiments, Subject 1.

included in curve B had been taken. The subject was then woken up, and, when apparently perfectly normal, an E.N.T. surgeon (Mr. R. K. Jones) was called in to see her. Without his having any detailed knowledge of the experiment, he was asked to examine the subject. His report was as follows:

History.—The patient was a married woman with two children. She made no complaint whatsoever of hearing disability. Her tonsils had been removed at the age of 18 months. She claimed to have been subjected to some excess of noise in her home—namely, the sound of an electric saw and drill, and musical sounds, her husband being a composer. She was fully awake and apparently in normal possession of her faculties, but, in the presence of a loud noise from electrical apparatus in the room, she made no response and seemed unable to hear it, although the noise was clearly audible to all present.

Membrana tympani: normal.

Response to ordinary speech: normal.

Response to tuning-fork (128 c/s): markedly reduced absolute bone conduction.

Vibration sense (medial malleoli, knuckles, and forehead): no response.

The first clinical examination completed, the subject was rehypnotized and cleared of all previous suggestions of deafness. She was woken up.

After a second clinical examination the surgeon then reported:

Weber.—Central.
Rinne.—+ Right and left.
Absolute bone conduction.—Normal.
Vibration sense.—Normal.
Hearing.—Normal.

Discussion

Apparent selective deafness to tones of specific frequency can be produced by D.S.U.H. in suitable deep-trance hypnotic subjects. There is also some evidence, as in the Table, to show that the actual words used when making the suggestions may have a special significance under hypnosis, even if this escapes the hypnotist and his subject when awake.

In psychological terms, we are dealing under hypnosis, almost by definition, with the unconscious mind. According to Freud's (1935) own account, it was while in Nancy in 1889, when watching Bernheim's experiments with hypnosis, that he first "received the profoundest impression of the possibility that there could be powerful processes which nevertheless remain hidden from the consciousness of men." In view of the inability of any of our subjects to distinguish significantly between "note" and "sound" in the waking state, it would appear possible that to the unconscious mind the semantics of the hypnotist's suggestions may have a special significance which remains otherwise hidden from consciousness. If this should be the case generally, in respect of all physiological responses produced by D.S.U.H. apart from those recorded in audiometry, it is hardly surprising that the clinical use of hypnosis has had up to date such a chequered career.

In particular our findings might presumably prove relevant when attempting the relief of a hysterical state presenting as a conversion symptom in the form of psychogenic deafness. In general they may also be relevant to all treatment under hypnosis and especially to the use of hypnosis by obstetricians for the production of anaesthesia during childbirth, when the unconscious interpretation of the semantics involved in such words as "you will feel no pain," for example, might possibly produce a number of unwanted physiological responses at the same time.

But the question still remains regarding the origin of the auditory experience of the subject who, presented with $\frac{1}{2}$ F_0 or 2 F_0 or other harmonic, is able to interpret this—for whatever psychological reasons—in terms of the frequency F_0, concerning which suggestions of deafness have been made. It might be argued that since 2 F_0 is a harmonic of F_0, this at least could have been presented unintentionally along with the test tone. Well aware of this possibility, however, we had included a filter in the circuit which, as stated above, would reduce 2 F_0 and any higher harmonic to less than 0.1%. In addition the effect of the filter itself was investigated, and it was found that its presence or absence made, in fact, no significant change in the subject's responses.

It must therefore be assumed that the responses were due to the presence of aural harmonics. However, although this might explain the subject's response to twice the test frequency, it is more difficult to find an adequate reason for any experience of half this frequency. Nevertheless, it could still be argued that when the test tone was $\frac{1}{2}$ F_0 the second harmonic then became F_0 itself, or the actual frequency of tone to which deafness had been suggested. It is therefore postulated that when the semantics of the suggestions conveyed to the subject the necessary information—whatever this may have been—the presence of F_0 as an aural harmonic of $\frac{1}{2}$ F_0 produced deafness to $\frac{1}{2}$ F_0 by association. A similar explanation could be offered to the finding of a single response of deafness to $\frac{1}{4}$ F_0.

We are dealing here, apparently, with some degree of auditory agnosia, but, while there is ample evidence of the genuine existence of aural harmonics (Egan and Klumpp, 1951; Lawrence and Yantis, 1956), there is no record of the subjects of such experiments reporting any

conscious experience of these harmonics. This being the case, the use of D.S.U.H. as a research tool in this field could open up the possibility of labelling the sensation of pitch as distinct from the total auditory experience, thereby facilitating research into the general mechanisms involved in hearing and the conscious distinction of different sorts of sounds.

The evidence of the conditioned-reflex experiments would seem to support the clinical and audiometric evidence that deafness to tones of specific frequency can be produced by D.S.U.H. However, it is recognized that the case is still, in some respects, unproved. Further work with conditioned reflexes, involving a variety of physiological responses other than heart rate, is now in progress.

Finally, it may be important that such selective deafness produced by D.S.U.H. appears to have been extended in all cases to include a loss of peripheral vibratory sense to the same frequency and in some cases to other frequencies. We are not, however, aware of evidence that any kind of deafness of psychopathological origins shows this association, but clinical investigation of this possibility could presumably settle the point.

Summary

The auditory thresholds of six deep-trance hypnotic subjects were measured in the waking state and again after deafness to tones of specific frequency had been suggested under hypnosis. This deafness was then further examined clinically and by means of experiments with positive conditioned reflexes, using heart rate as the conditioned response. In certain subjects this selective deafness sometimes included not only the test frequency but also half and occasionally twice this frequency, and on one occasion one-third of the frequency. Some evidence was found to support the thesis that these variations in responses were related to the semantics of the words used by the hypnotist when making his suggestions, although the subjects were not aware of any such distinctions in the waking state. There was also evidence of an associated loss of peripheral vibratory sense to the same frequency as the test tone, and in some cases to other frequencies.

Our thanks are due to Dr. A. Spencer Paterson for his help and for the facilities provided in the Psychiatric Department of the West London Hospital, and to Dr. O. G. Edholm for the use of laboratory space and equipment in the Division of Human Physiology of the Medical Research Council. We also gratefully acknowledge the valuable technical assistance in respect of the conditioned-reflex experiments provided by Mr. D. Passerini, Dan Mason Research Scholar in the Psychiatric Department of the West London Hospital. The work was supported by grants from the Medical Research Council and from Ergonomics Limited; and apparatus was provided by the Medical Research Council, the Physiology Department of the Charing Cross Hospital Medical School, the British Broadcasting Corporation, and the Dan Mason Research Foundation.

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CONGENITAL ICHTHYOSIFORM ERYTHRODERMIA TREATED BY HYPNOSIS

REPORT OF TWO CASES

BY

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[WITH SPECIAL PLATE]

A novel and spectacularly successful approach to the treatment of congenital ichthyosiform erythrodermia (Brocq, 1902) was made when Mason (1952) treated a patient by direct suggestion under hypnosis. The clinical diagnosis had been confirmed by biopsy. Except for the skin of the chest, face, and neck, the whole body of the patient, a boy of 16, was covered by a thick, blackish horny layer. Transplants by plastic surgery of apparently normal skin from the chest soon became ichthyotic in their turn, and contractures resulted. However, five days after hypnotic suggestions of improvement had been given the horny layer started to soften and be shed, but only in that area to which the suggestions applied. It therefore seemed improbable that the resolution had occurred spontaneously. Subsequently the other affected areas were included in suggestions of cure, and showed a similar response. The improvement, assessed at between 95% and 50% in different parts, had been maintained four years after treatment had been completed (Mason, 1960). Mason concluded either that there is a hitherto unrecognized psychic factor in the aetiology of the disease or that a congenital organic condition had been affected by a psychological process, or that a combination of both these factors obtained.

Schneck (1954) used hypnosis in treating another form of fish-skin disease, a case of ichthyosis simplex in a 33-year-old man whose whole body was affected to a varying degree and who suffered the typical winter exacerbation. The patient was rather sceptical of hypnotherapy at first, and tended to underestimate the beneficial results which seemed attributable to it. These results were variable and irregular, but the patient largely escaped the next cold-weather deterioration. When his attitude of "healthy scepticism" was altered to one of strong desire to prove responsive to treatment there was an over-all improvement assessed at between 40% and 45%. The patient himself related the efficacy of the treatments to the depth of the trance state achieved on each occasion. Schneck commented on the significance of this attitude, and remarked on the need for biochemical and physiological investigations with the experimental use of hypnosis in ichthyosis and other skin disorders.

Two further cases of congenital ichthyosiform erythrodermia treated by hypnosis are described here. The patients are sisters; there is no family history of this or any other ichthyotic manifestation or ectodermal defect. Twin brothers delivered at home in May, 1960, appear so far to be normal, and there are no other siblings.

Case 1

The patient, a female, was born at full term by spontaneous delivery after a normal pregnancy on March 8, 1952. At birth the skin of the trunk, palms, and soles was seen to have a dusky-red hue, but the infant was otherwise normal in appearance. No peculiarity of the vernix caseosa

was noted. In a few weeks the skin started to become rough and flaky. The condition gradually and progressively worsened, so that by the end of the seventh year the whole integument was thickened and scaly, especially in the antecubital fossae, the popliteal fossae, and the anterior surface of the neck. This predilection for flexor aspects is characteristic of congenital ichthyosiform erythrodermia and serves to differentiate it from other forms of ichthyosis. The skin of the palmar aspects of the fingers and hands, and that of the plantar surfaces of the feet and toes, was covered by rigid horny plates with cracks and fissures overlying every joint; these were especially painful at the metacarpophalangeal joints. The nail growth was normal. The skin of the trunk and front of the neck was thickened and greyish and formed small rectangular scales very like those of lizard skin; on the legs the scales were thinner and much larger. Sometimes neighbouring scales separated and raw gaps forming a reticulate pattern appeared, these being particularly painful and distressing. The skin of the face showed a branny desquamation. The mucous membranes were normal and the teeth properly developed though carious. Hair growth was also normal, but the scalp was the seat of thick seborrhoeic crusting. One unusual, if not unique, feature was that the skin became thicker in summer, and would desquamate and remain thinner during winter; this is in direct contrast to the usual course of events consistently described.

Case 2

This patient, born normally on July 4, 1954, presented features similar to those of her sister, except that the erythrodermia was much less marked and there was no hyperkeratosis of the palms and soles. Ichthyotic changes were otherwise identical in form and distribution, but less severe throughout, except on the anterior surface of the neck. Both children were of average intelligence, seemed content and well adjusted in spite of their disfigurement, and were co-operative.

Previous treatment had included applications of ung. adip. lan. hydros. containing 10% sodium chloride (Ljungstrom, 1941), and occasional intensive courses of vitamin A by mouth in a dosage of 150,000 units daily (Rapaport, Herman, and Lehman, 1942). The former kept the skin reasonably supple, and the latter would bring about a phase of desquamation and a noticeable temporary improvement, but the condition would relapse after a fortnight or so, and for a short while afterwards the skin would be rather worse.

Response to Treatment

Treatment by direct suggestion under hypnosis was begun on February 27, 1960, when the appearances in Case 1 were as shown in Special Plate, Fig. 1. This patient was induced readily by the eye-fixation technique, and the trance state deepened with arm levitation. Skin analgesia of the right arm was then produced and demonstrated in order to heighten suggestibility, and normal sensation returned two minutes after "waking" as a result of post-hypnotic suggestion. This indicated that the patient had at the first session entered a fairly deep trance state. Direct suggestion was made under hypnosis that the affected skin of the right forearm, hand, and fingers would soon start to grow soft and smooth and the thick skin would flake off. This suggestion was repeated at weekly intervals for eight weeks, and intentionally restricted to that area for purposes of comparison with the left. Thereafter at fortnightly intervals for the next two months, and then monthly for a further two months, the suggestions were extended to include the whole integument.

Fourteen days after the treatment was started the patient claimed that the fingers of both hands equally felt softer and that "she could feel things more easily"; there was, however, no objective improvement at this stage. After 28 days the skin of all finger-tips was noticeably thinner and less scaly and the palms of both hands softer; the horny layer was thinner and more flexible. These changes were slightly but definitely more marked on the right limb—that is, on the side to which the therapeutic suggestions exclusively applied. By the end of the sixth week the rate of improvement had increased, the skin of the terminal phalanx of the right thumb being entirely normal in texture, and that of all the other terminal phalanges of the right hand practically so, though still erythematous. The improvement on the left side was slightly less striking. There were several areas of clearing on both palms. At the end of the eighth week the improvement had continued and there were penny-sized areas of normal skin in the centre of each palm, as well as evidence of mitigation elsewhere. Subsequently the whole skin was involved in suggestions of improvement (not of cure), and within a fortnight flakes were being shed from the abdomen. Her mother remarked that she was now much easier to keep clean. By April 29, 1960, the exceptional weather was, according to previous experience, warm enough to have brought about a considerable worsening of the skin condition instead of the improvement now noted, and this continued in the unusually warm early summer that followed. In July the general condition of the skin had not been better since infancy, but branny flakes persisted on the trunk and limbs and to a less extent on the face (Special Plate, Fig. 2).

Case 2 never entered a deep trance state, and did not enter one of medium depth until the fourth session. No improvement resulted until after this session, when it had been suggested that the skin of the face and front of the neck would grow softer and smoother. At this stage the skin of the forehead did in fact start to clear from the centre. A week later this process had extended on the forehead and also on the chin and round the mouth. The skin on the front of the neck was also softer. By the sixth week the clearing of the face was striking, and by the tenth week the skin of the face and legs was practically normal, though suggestions had not included the legs in this case. The skin of the trunk was also slightly better, but no further improvement could be achieved, though this patient too escaped her usual hot-weather deterioration.

Attempts at the assessment of skin changes can never be accurate and may be misleading. Photographic comparisons may also be deceptive unless the pictures are taken under identical conditions of lighting and other contrast techniques. With these reservations, the improvement in these two cases is tabulated as follows:

Table Showing Clinical Assessment of Improvement

	Case 1		Case 2	
	Reduction in Skin Thickness	Reduction in Area Affected	Reduction in Skin Thickness	Reduction in Area Affected
Face	50%	25%	75%	90%
Neck	75%	0	40%	0
Arms	50%	0	20%	0
Palms and fingers	50%	50%	—	—
Trunk	50%	0	25%	0
Legs	75%	75%	20%	0
Soles and toes	50%	50%	—	—

Discussion

These results show features in common with those of both previously reported cases. There is apparently some correspondence between specific suggestions and the changes consequent upon them. In Mason's case this correspondence was very striking, and seems to indicate the influence of a psychological process acting directly on local tissue metabolism. The condition so affected is undoubtedly congenital and hereditary (Cockayne, 1933), and it is difficult to see by what pathways such an influence could be mediated. On the other hand, the psychotherapeutic approach of Schneck, not aimed primarily at symptom-removal, can be more easily understood to exert a generalized beneficial effect, rather than a local and specific effect, on any organic

condition associated with psychological factors. There is, however, no evidence that there is any constant primary psychopathic or psychoneurotic component in the ichthyoses, except in the case of some of the variants of Rud's syndrome, where congenital ichthyosis is associated with spastic diplegia and mental deficiency (Richards, 1960).

In the two cases described above it seemed unlikely that there was a psychological factor in the aetiology, and both showed some definite conformity to the suggestions, though this conformity was not exact, for the response included improvement extending outside the designated areas, and a relative failure in other areas which were intended to respond. Finally, though there was a mild improvement in undesignated areas, it was quite overshadowed by the changes in those intended to benefit.

As Schneck's patient commented, and as shown by the subjective response of Case 1 and the objective response of Case 2, there seems to be some relation between depth of trance state and efficacy of suggestion. This could be explained if it were generally true that suggestibility is enhanced in proportion to the depth of the trance state in hypnosis. This, however, is certainly not true in the "charming away" of warts, for here if the suggestion is assertive enough it is likely to be effective, whether hypnosis is used or not.

If, therefore, the credulity or suggestibility of the subject does in fact exert an influence on the outcome, it would be logical to use all possible means to increase this suggestibility. Nevertheless, in most cases emphatic and optimistic assertions of cure by hypnosis remain morally indefensible so long as the outcome is in fact uncertain, while to give the subject a more sanguine prognosis is to spike one's own guns by undermining the authority behind one's suggestions.

While there is at present no clear solution to this dilemma, there can be no doubt that hypnosis has a rightful and potentially important place as an ethical therapeutic measure in this and in many other conditions.

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Hong Kong 1960, the Colony's annual report, reviews the fascinating subject of the water supplies of a community with a total land area of 398 square miles, no natural lakes or large rivers, a summer rainfall of around 85 inches, and a population which has risen from 90,000 when the first reservoir was planned in 1895 to a figure now thought to be in the region of 3,200,000. Reservoir after reservoir has been built, and yet demand is continually overtaking supply. The latest schemes to be embarked on will cost over $1,225m. in the next ten years, and will practically exhaust conventional sources of supply. If the demand still grows, the report says that it can only be hoped that the use of nuclear power to distil sea-water will by that time have become an economic proposition. However, in spite of the restricted water supply, the overcrowding, and the rapidly increasing population, the Colony's general health has remained remarkably good. (H.M.S.O., 12s. 6d.)

TREATMENT OF PLANTAR WARTS IN CHILDREN

BY

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Plantar warts are often thought to be trivial lesions, but they are a very real cause of disability in childhood. There appears to have been a rapid rise in the incidence of such lesions, Horwitz and Marker (1960) noting a fivefold increase in the past 25 years. Treatment is time-consuming and often disappointing, and, as the spontaneous cure rate may be as high as 27% in three months, assessment of results is difficult (Horwitz and Marker, 1960).

Over the years many treatments have been tried. Curettage is probably the oldest and remains popular. It can give good results in the hands of experienced dermatologists, but a painful scar may result (Duthie and McCallum, 1951). Apart from this, the injection of a local anaesthetic into the sole is almost always painful and often there is considerable discomfort for several days after the operation, especially if the silver nitrate stick is used as a haemostatic. Radiotherapy was used to a large extent in the armed Forces during the second world war, but has fallen into complete disrepute owing to the reports of disastrous after-effects (Shaw, 1948; McLaughlin, 1948). Duthie and McCallum (1951) used occlusive "elastoplast" dressings combined with podophyllin and cured 60% of their patients in two months. This method is time-consuming to the medical attendant and probably entails frequent visits to hospital or surgery; also, the cure rate seems disappointingly low. Morgan (1952) used liquid nitrogen in the treatment of 14 patients, of whom 10 were cured. In our experience this method is associated with considerable pain and a high recurrence rate.

In 1943 Thomson, using 3% formalin solution for hyperhidrosis, made the accidental discovery that plantar warts responded to such treatment. He reported a 75% cure rate in a small group of patients, though Warin (1958), using a slightly different technique, cured only one-third to one-half of his patients. The results with formalin are entirely dependent on the co-operation of the patient and the enthusiasm of the doctor in encouraging persistence with treatment. With these facts in view it was decided to undertake both a retrospective and a prospective survey of the results of treatment with formalin in this department.

Material

Retrospective Survey.—Between January, 1957, and January, 1959, 465 children under 17 years of age had been treated for plantar warts. All were contacted by letter and were asked to attend the department for personal review between July and September, 1960 (an average follow-up period of 2.7 years, with a minimum follow-up of 1.5 years): 391 (84.8%) attended as requested, a further 55 (11.1%) replied by letter giving sufficient information for the study, and only 19 (4.1%) remained untraced.

Prospective Survey.—A series of 200 consecutive patients (148 girls, 52 boys) with plantar warts who were

under the age of 17 were treated with formalin for up to 16 weeks: 74% were between the ages of 10 and 14; only three were less than 5.

Technique

In the initial stages of treatment 3% formalin solution was used. The patient was instructed to remove scale and dead tissue from the top of the wart by scraping with a nail-file or the side of the blade of a pair of scissors. The wart-bearing portion of the sole was then soaked in the solution for 15 to 20 minutes (it is important to stress that the wart must not be placed in contact with the bottom of the receptacle). The whole process was repeated each night. Several patients developed interdigital cracks due to hardening of the skin. To prevent this, if the warts were near toe clefts the patients were instructed to place a little petroleum jelly between the toes before starting treatment. If there was little hardening of the skin after three weeks' treatment the formalin was increased to 5%, 7%, or even 10%.

Results

Retrospective Survey.—In this series 407 (91.3%) of those traced were cured at the first attempt, while 39 (8.7%) had suffered recurrence or reinfection (warts appearing at a different site at least six months after the original lesion had cleared). Only two methods of treatment had been used during the period under review, and the results are shown in Table I. The cure rate was higher and the recurrence rate much lower in the group treated with formalin at some stage. The recurrence rate after curettage did not depend on the experience of the operator. There were seven cases of reinfection after curettage alone but none in those treated with formalin. Only 31 patients whose warts were removed with the curette had visible scars and only two were painful.

TABLE I

Treatment	Total	Cured	Recurrence	Reinfection
Curettage alone ..	102	65	30	7
Formalin	223	222	1	—
,, followed by curettage ..	121	120	1	—

Prospective Survey.—In this series 191 (95.5%) patients were cured by formalin. In seven, formalin treatment was abandoned after 16 weeks and the warts were curetted, as it was felt that no useful purpose would be served by continuing. Two patients developed contact dermatitis due to formalin, and, though they are classed as failures, the violence of the local reaction caused the death of the warts. The average time taken to clear the warts in the successful patients was 8.2 weeks. Age and sex bore no relation to the time required, but a definite relationship existed between the child's weight and the time taken for clearance (Table II). The weights were adjusted for height and age from tables of Mitchell Nelson (1945). Further analysis of those patients needing more than eight weeks to clear showed that, in addition to excess weight, many had large warts (greater than 1.25 cm. in diameter), either solitary or multiple, or mosaic warts. Of warts less than 1 cm. in diameter 80% were clear after eight weeks' treatment. There was no obvious relationship between the length of time taken for cure and the time the warts had been present. Each patient was carefully questioned in an attempt to find the source of infection. In 32 the only possible source of infection was bare-foot dancing or physical training at school; 30 of these were girls, and it seems that few if any boys' schools indulge in such practices.

TABLE II

Child's Weight	Time Taken to Clearance
25% underweight (35 children)	5·6 weeks
Average weight (122 ,,)	6·7
25% overweight (34 ,,)	9·3 ,,

Discussion

When the first group of children were treated the routine therapy for multiple plantar warts was formalin, but many solitary warts were curetted without prior formalin therapy. The results of the survey clearly demonstrated the value of such prior therapy in the prevention of recurrence and reinfection, but it was impossible to deduce the optimum length of treatment with formalin or to estimate the true cure rate with such treatment.

In the second group of children, treated with formalin alone for up to 16 weeks, the child's weight was the only factor constantly related to the time needed for cure; presumably this is due to increasing skin thickness on the sole with increasing weight.

Excluding patients with very large or mosaic warts and those occurring in overweight children, the length of treatment justifiable appears to be six to eight weeks, by which time 80% of all warts up to 1 cm. in diameter will be cleared. Any present after this should be curetted. Solitary or multiple large warts may respond in this time (48%), but it seems wise to curette such lesions after three weeks' treatment with formalin, by which time about 25% will be cured and the remainder will not be liable to recurrence or reinfection.

It is difficult to explain the lower recurrence and reinfection rate after formalin therapy. It may be that many of the so-called reinfections and recurrences merely represent the continuous growth of other warts present in microscopic size when the original wart was treated. Formalin is extremely effective in dealing with small warts, and it is probable that it cures such microscopic warts.

The advantages of formalin therapy are therefore considerable, but it must be remembered that technique is all-important. Many of the patients in the second series had been treated with formalin before attending the department, but 45% of these had not used the correct technique, variations ranging from holding the uncorked bottle of formalin solution over the wart (a difficult manœuvre) to soaking the foot once a week or merely placing pads of cotton-wool soaked in formalin over the wart for a minute a day (cf. Warin, 1958). The correct treatment is time-consuming, but five minutes spent with the patient at the first visit explaining the advantages of the method will usually ensure co-operation.

Summary

As a result of a survey of 646 children with plantar warts, it is shown that formalin foot-soaks used for 15 to 20 minutes each night for six to eight weeks will cure 80% of all plantar warts up to 1 cm. in diameter. Larger warts should be curetted after three weeks' treatment with formalin. By these means the recurrence and reinfection rates are reduced to extremely low levels. The other advantages of the method are its simplicity and painlessness.

I thank Drs. I. B. Sneddon and R. E. Church for permission to treat their patients and for much advice and encouragement. I also thank the parents and children in the second series for their patient co-operation.

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"MONDAY HEAD": AN INTERESTING OCCUPATIONAL DISORDER

BY

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It has been recognized almost since the first introduction of organic nitrates into therapeutics that these compounds are capable of producing headaches.

It is a common experience of the physician that patients with angina pectoris who are under treatment with these compounds have headache as a leading side-effect. However, this is of little importance in practice, partly because habituation occurs readily (Goodman and Gilman, 1955; Laurence and Moulton, 1960) and partly because the therapeutic response producing relief from anginal pain overshadows the discomfort of the side-action.

Industrial workers handling nitrates may absorb sufficient through the surface of the body to produce symptoms, the commonest of which is headache. This, too, has been known for many years, the first description of the effect being published in 1910 (Laws, 1910). Since no therapeutic effect is intended in these cases and since the substance is introduced into the body accidentally, one may legitimately call this an industrial disease referable to chemical toxicity.

There have been many instances of "nitrate head" reported in the literature, the greatest incidence of the condition being just before and during the two world wars, when production of explosives was at its peak. It is indeed interesting to note that the earliest report on nitroglycerin-induced headache is attributed to an Army officer serving during the Boer War (Ebright, 1914). All publications hitherto have understandably dealt with the characteristics, mode of prevention, and treatment of this troublesome disorder produced by nitroglycerin in munition workers, Service men, and miners (Laws, 1910; Ebright, 1914; Rabinowitch, 1944; Schwartz, 1946; Forssman *et al.*, 1958). There have been no accounts of the condition affecting workers using different nitro-compounds in other occupations, and this paper describes, for the first time, nitrate headache in workers in a pharmaceutical manufacturing plant where a new coronary-artery dilator drug was being made.

Basically, the process consisted of the nitration with aqua regia of the dianhydro derivative of sorbitol to produce isosorbide dinitrate, which was then recrystallized from absolute alcohol. After filtration through sintered glass the salt was dried on trays in a vacuum oven at room temperature. When dry the powder was scraped by hand from the trays into glass dishes, in which it was passed to another laboratory for compounding into tablets containing lactose. The final product is a tableted form of the active compound intended for human experimental therapeutics.

The three cases reported below occurred in the development laboratory where the isosorbide dinitrate was in preparation. The manufacturing process was conducted by a team of three men.

Case 1

The subject was a male chemist aged 31 who had always been fit and was not particularly prone to headaches in the ordinary course of events. He was well built and apparently in normal health at the time of starting work in the nitrate plant. He began synthesizing isosorbide dinitrate on the morning of Thursday, April 20, 1961, and continued full-time at the process, working from 9 a.m. to 5.30 p.m., with a break of one hour for lunch, until the afternoon of Saturday, April 22, at 1 p.m.

He was apparently well until 11 a.m. on Saturday morning when he first developed headache, which persisted on that day until 2 p.m. He had no headache on Sunday. On Monday morning, April 24, he started work on the process again and continued full-time each day, being first seen on Thursday, April 27. He gave a history of recurrent headache which reappeared on Tuesday, April 25, and which he experienced every day that he was in the nitrate plant.

The headache occurred about mid-morning and persisted for the rest of the day until he went to bed at night; it dispersed overnight and he felt well each morning until about 11 a.m. Although not severe it caused sufficient discomfort for him to take 5 gr. (0.32 g.) of aspirin. Relief was attained for about 15 minutes on the one occasion that he took the analgesic. The ache was bitemporal in site, it was persistent, and was not throbbing. There was no lancination, and he described it as being "like pressure on each temple." There were no other symptoms at the time; he was not nauseated, nor did he experience tinnitus, vertigo, palpitations, or flushing of the skin.

He always washed his hands thoroughly before meals, did not smoke during working hours, and handled the active compound relatively little. The route of entry of the substance is difficult to trace with certainty; inhalation is a possibility, since the compound is dried from absolute alcohol and it is possible that isosorbide dinitrate dust was present in the atmosphere.

Case 2

A male chemist aged 28 who always enjoyed good health had been employed as an ammunition examiner in the Army between the years of 1951 and 1954, when he was doing his national service in the Middle East. During this employment he had been accustomed to handling guncotton and other explosives in the form of many common varieties of land-service explosives. He experienced headaches during his tour of duty when handling these nitro explosives. He and his fellow Service men called the attacks "N.G. heads," which they regarded as of nuisance value only and which they treated by lying down in a darkened room and drinking cold beer. This method of treatment achieved great repute in the Canal Zone of Egypt.

He began operating in the nitration plant on Wednesday, April 19, at 9 a.m. He first noticed headache on Friday, April 21, during the morning. He recognized the symptom

quite soon as being like "N.G. head." He was well during the two days of the week-end, but there was a recurrence of headache on Monday afternoon, April 24. Since that time he experienced headache each day, the symptoms beginning at about 3 p.m., persisting until he retired to bed at night and recurring about the same time the following day. During week-ends he was asymptomatic; the severity of the headache, while not being great at any time, was more severe during the first week of exposure to nitrate than during the second week.

The site of the discomfort was retro-orbital, bitemporal, and occipital. It was constant in site without radiation and had a dull aching character with occasional lancinating. It was not pulsatile and it was not associated with other symptoms. In particular, no nausea, no vomiting, no visual disturbances, and no auditory symptoms occurred. He was not unduly perturbed by the headache, although he took 10 gr. (0.65 g.) of aspirin on one occasion during the first evening that he had the symptom. This dose of salicylate effectively removed the discomfort for about 15 minutes but did not have any longer-lasting action.

This worker was a qualified organic chemist without any relevant previous medical history, and he always washed well after leaving the nitration plant for meals. He neither smoked nor ate sweets while working. The source of entry of the nitrate in this case is almost certainly by inhalation, since he was not touching the active compound to nearly the same extent as the first subject.

Case 3

A chemist aged 34, this man was always fit and usually free from headaches until he began work on the production of organic nitrate.

He began operations at a later date than the first two subjects and was exposed to the inhalation of nitrate dust, and presumably fumes too, for some hours of his first day in the plant. The day in question was particularly hot and he developed a severe pulsatile headache within three hours of first exposure to the compound. The ache was sited mainly on the top of the head, but there was occipital radiation and some pain in the frontal region. The headache became steadily worse, although he was able to go on working until the end of the day. During the evening it became severe enough to make him anorectic and unable to do more than sit quietly in a chair until it was his usual bedtime. He was unable to sleep properly because of the headache, which gradually diminished during the night and disappeared by the following morning. At its height the headache was associated with a "full" feeling in the head, palpitations, lethargy, and difficulty in mental concentration. The worker did not notice flushing of his skin. During the following day, which was also hot, he again had a very severe headache and complained to those in charge of the plant so that attention was drawn to the condition, thus initiating adequate preventive measures.

With the introduction of exhaust ventilation, the provision of a change of clothing, and the use of shower-bathing at the end of each working period in the nitrate plant, this distressing occupational syndrome did not recur.

Discussion

The syndrome of nitrate-induced headache is characterized by a distressing headache which may be constant and aching but more typically is pulsatile, and which, when severe, is associated with "fullness in the head," palpitations, anorexia, nausea, faintness, tinnitus, mental confusion, flushing of the skin, and, occasionally, visual disturbances (Laws, 1910; Rabinowitch, 1944; Schwartz, 1946). The headache is made worse by stooping and lying down (Rabinowitch, 1944).

The disorder may be encountered in differing degrees of severity, differences between cases probably being accounted for by degrees of habituation and differences in the amount of nitrate absorbed as well as by differences in individual susceptibility.

There is a constant aetiological association with exposure to nitrate dust and fumes. The speed and power of action of the compound are to a certain extent related to the weather, especially the ambient temperature (Ebright, 1914).

These characteristics are referred to in the several popular synonyms for this interesting condition—for example, "nitrate head," "N.G. head," "powder head," "Monday headache." The last-mentioned term derives from the loss of habituation which occurs during a week-end free from exposure; the other terms have, of course, aetiological significance.

The syndrome is troublesome, although of itself it has little serious prognostic significance for the affected worker (Forssman *et al.*, 1958). However, it is known that alcohol and nitrates are mutually potentiating, and there have been several instances where an individual with nitrate intoxication has gone berserk after taking alcohol (Jennings, 1903; *Brit. med. J.*, 1903; Laws, 1910; Ebright, 1914; Forssman *et al.*, 1958). In a few cases homicide has been committed during the temporary lapse (Ebright, 1914; Hamilton, 1925; Rabinowitch, 1944). For this reason alone the occurrence of the disorder demands the most strenuous efforts on the part of all concerned to eradicate the conditions allowing it to develop.

Workers themselves have discovered that habituation is readily produced (Ebright, 1914; Schwartz, 1946; Modell, 1960), and there have been many cases of men spending 25 years in a nitrate plant, having overcome the initial discomfort associated with exposure (Laws, 1910). These "old hands," realizing the ready loss of habituation that occurs during week-ends away from the plant, are known to rub a little of the nitrate into their hat-bands so that they absorb sufficient when off work to maintain the state of habituation (Schwartz, 1946; Sax, 1951; Goodman and Gilman, 1955).

The alleged aphrodisiac action of nitrates (Laws, 1910) would seem to provide little compensation for the worker with a pounding headache and nausea despite the effect on fertility that these substances are supposed to have (Laws, 1910).

The pathogenesis of the syndrome is referable to the effect of nitrate ions on the arterioles. The headache is probably due to cerebral vasodilatation and a rise in intracranial pressure (Schwartz, 1946; Goodman and Gilman, 1955; Laurence and Moulton, 1960). The mode of entry of the nitrate is either through the skin or by inhalation, or possibly by both routes.

It has been suggested that a psychic factor may be involved in the production of these headaches, since many workers subject to the syndrome realize the danger of handling these explosive substances and may even have witnessed the sudden death or maiming of their colleagues (Schwartz, 1946). However, this is almost certainly a subsidiary and contributing factor to a primarily organic disorder.

The disorder may be prevented by the use of protective clothing, adequate removal of dust and fumes from the workplace (Forssman *et al.*, 1958), and by limiting, so far as is possible, the amount of these produced during milling of the offending material. Prevention is thus a matter of elementary industrial hygiene.

Summary

The occurrence and causation of nitrate-induced headache in industrial workers are reviewed, and three cases occurring in a pharmaceutical manufacturing plant are described. The mode of production of this troublesome syndrome and the ease with which it may be prevented are outlined. The relevant literature is reviewed in the context of the account.

We are indebted to Dr. L. F. Wiggins, Director of Research at the Nicholas Research Institute, for permission to publish this account. Thanks are also due to Dr. F. G. M. Seager, of Slough Industrial Health Service, for his ready co-operation in the investigation of the cases reported.

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Medical Memoranda

Pneumatosis Cystoides Intestinalis

Until recently the condition of pneumatosis cystoides intestinalis had rarely been described as involving the large bowel. In only 9 out of 213 cases reviewed by Koss (1952) was the colon the sole site of the disease; the majority involved the small intestine and its peritoneal attachments.

When the large bowel has been implicated, the condition has usually been recognized as the result of symptoms either of dysfunction or of mechanical obstruction of the bowel, directly attributable to the presence of the cysts. This contrasts to the so-called "secondary pneumatosis" of the small intestine related to other pathological processes such as peptic ulceration or neoplasm, which are the prime cause of symptoms. In the large bowel, although previous sigmoidoscopy or minor operative procedure such as polypectomy has been the implied causative factor in the production of the cysts (Marshak *et al.*, 1956), the condition may develop spontaneously. To such cases the term "primary pneumatosis" may accurately be given, and an increasing number of such examples have appeared in recent years in the literature.

The presence of gas cysts affecting the sigmoid colon, and associated with recurrent volvulus of the affected loop, was reported by Jones (1948). Resection was performed in this patient. Witkowski *et al.* (1955) described a case where symptoms of large-bowel obstruction led to the diagnosis, again with resection of the affected portion of bowel as the outcome. A disturbing feature was the later appearance of further cysts in the remaining colon, with no evidence of a tendency to spontaneous remission. Griffiths (1955) reported a case in which pain in the left iliac fossa and passage of mucus and blood per rectum were the presenting symptoms. Diagnosis was made on radiological and sigmoidoscopic findings, and later subacute obstructive symptoms supervened, necessitating resection of the affected bowel. Shoesmith and Crone (1959) have treated two further patients in whom the left colon was involved; in one the cystic changes extended into the rectum.

We record below yet another example of severe pneumatosis cystoides intestinalis affecting the left colon and presenting as a volvulus of the involved loop.

CASE REPORT

The patient, a man of 38 and a known severe epileptic, was admitted to hospital on January 18, 1959. He gave a history of severe lower abdominal pain of sudden onset, occurring while he was in bed three hours before admission. He had vomited once, immediately after the onset of the pain, and stated that for the previous three days his motions had been "rather loose."

The past history was difficult to assess as he was of low intellect, being cared for at home by his sister. He had never worked, and epileptiform attacks were frequent despite prolonged and heavy drug treatment. There was no history of dyspepsia or of previous abdominal pain. His sister volunteered the information that he tended to be constipated and had been known to introduce foreign bodies into his rectum.

On admission he was found to be a poor witness, in some pain, but this was apparently much less severe than at the onset. The abdomen was distended, but without rigidity or localized tenderness. Rectal examination showed no evidence of any foreign body or local trauma, and the rectum was empty. His general condition was good, with no evidence of shock. Plain *x*-ray films of the abdomen in the erect and supine positions demonstrated considerable distension of the large bowel, without the presence of fluid levels. No faecal result was obtained from two enemas.

After admission his pain subsided and it was decided to pursue a conservative regime. There was no further vomiting, and he became less distended, with passage of flatus and some fluid faeces per rectum. Pain recurred, however, and on January 22 a small amount of barium was run into the rectum. This demonstrated an apparent complete obstruction at the recto-sigmoid junction. The barium was retrieved, and sigmoidoscopy demonstrated an impassable obstruction at 20 cm. from the anal margin. It was thought that he had either a recurring volvulus at the recto-sigmoid junction or an impacted foreign body. Laparotomy was performed.

At operation a volvulus of the sigmoid loop through 180 degrees was found to have occurred. The loop of bowel involved was greatly enlarged, but it untwisted readily and was perfectly viable. On examination the affected loop was found to be the site of multiple gas cysts, encroaching on the lumen and projecting on the serosal surface. The rectum and rest of the bowel were quite normal in appearance, there being no evidence of any coincidental lesion in the stomach or intestine. Attempted deflation resulted in very little diminution in the size of the bowel, and the affected portion was resected by the Mikulicz procedure.

HISTOPATHOLOGY

The resected bowel consisted of sigmoid colon, measuring 40 cm. in length, and 13 by 9 cm. in cross-section at its largest part, after fixation. The great increase in diameter was due to the large number of gas-filled cysts situated in the bowel wall, giving the specimen a spongy consistency on palpation.

The gas was completely confined to the cysts, and could not be forced from one cyst to the next or into the lumen of the colon. The cysts could be made to rupture on moderate pressure.

The cut surface (Fig. 1) showed solitary cysts up to 5 cm. in diameter, but most were divided into smaller cavities by thin white septa. The largest multilocular cyst was 8 cm. in diameter, and the smallest 0.4 cm. All the cysts had a smooth, white glistening internal surface, and were empty of any solid or liquid content. The mucous membrane of the colon appeared normal and the lumen was not appreciably narrowed.

There was no macroscopic evidence of neoplasm or inflammation, other than some congestion of the external surface.

Histological sections (Fig. 2) demonstrated that the cysts occupied the submucous layer, between the muscularis mucosae and the inner circular muscle layer of the colon. The cysts were subdivided by thin fibrous septa, lined for the most part by a thin single layer of flattened cells, resembling endothelial cells. These cells contained elongated nuclei and eosinophilic cytoplasm. In a few places the endothelium appeared incomplete, and in other places assumed cuboidal form.

Moderate numbers of multinucleate foreign-body giant cells were present in the lining of the cysts. These ranged from elongated cells with two or three nuclei to large giant cells with thirty or more nuclei. All gradations were seen, from the single flat endothelial cell to the large giant cell. These giant cells were more numerous towards the mucosal side of the specimen, and some appeared to be partially detached from the wall of the cyst.

FIG. 1.—Resected specimen of sigmoid colon.

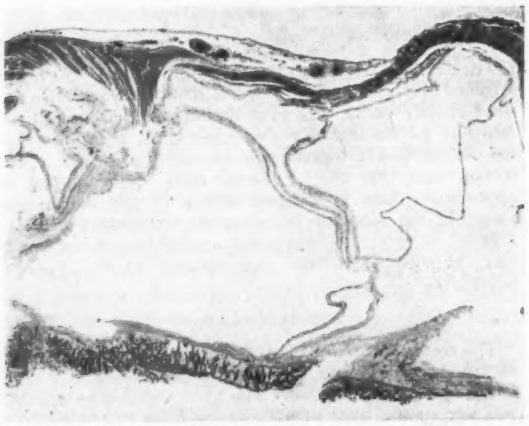

FIG. 2.—Low-power photomicrograph, showing gas cysts in the submucous layer. There is evidence of congestion of the serous coat.

The serous coat showed oedema, early acute inflammatory change with congestion, and diapedesis of polymorphonuclear cells. Dense focal accumulations of acute inflammatory cells were present. The mucous membrane showed oedema, with early and superficial ulceration of the epithelium in places. These latter changes were probably related to the volvulus. The patient's progress after operation was slow, principally owing to increasing epileptic attacks and deterioration in his mental condition. The double-barrelled colostomy was closed by intraperitoneal technique on February 19, and opportunity was taken for re-exploration of the abdomen on that occasion. No further cysts were seen in remaining bowel.

Further deterioration in his epileptiform state necessitated his remaining in hospital until April 28. At that time his bowels were open regularly and he had no abdominal symptoms.

COMMENT

In considering the pathogenesis of pneumatosis cystoides intestinalis several theories have been advanced. Some are substantiated by factual evidence, others are purely conjectural. The condition has been described in infants, but must be regarded as an acquired rather than a congenital disorder. In a series of infants reviewed by Paris (1955) the gas cysts were invariably associated with an acute enteritis.

It is generally accepted that the cysts represent distended lymphatic channels, both on the evidence of the position of the cysts and on their histological appearance. However, no truly satisfactory reason for the gaseous distension has been advanced and proved without doubt.

Of the many theories, the mechanical one impresses most. Here it is postulated that a breach in the intestinal mucosa allows the abnormal entrance of gases, which permeate into near-by lymphatics. Increased intraluminal pressure, admittedly of doubtful origin, serves to increase the gaseous influx, with consequent distension of the resultant cysts by a purely mechanical process. Such breaches in the mucosa occur in the presence of intestinal ulceration or neoplasm, in enteritis, and after such procedures as sigmoidoscopy and polypectomy. If this is so, it is surprising that the condition has not been recognized more often, though this may be due to the rapid disappearance of gas cysts by a process of gaseous absorption or rupture. Such a theory would explain the not infrequent occurrence of spontaneous pneumoperitoneum recognized as an incidental finding while radiological studies of the abdomen are being made.

A possible explanation is that an alteration occurs in the permeability of the mucosa. This may result from the presence of near-by disease, enteritis, or a nutritional deficiency. In support of the latter, a condition of pneumatosis of the intestines of swine has been produced experimentally by feeding them solely on a diet of polished rice.

It may be reasonable to combine the mechanical and disordered permeability theories. An increased intraluminal pressure, occurring for example during defaecation, vomiting, or at sigmoidoscopy, may well increase the tendency to gaseous diffusion in a mucosa already of suspect permeability.

Whether or not cysts arise secondary to an episode of intestinal obstruction is a matter for conjecture. Sauser-Hall (1940) suggested that this might be so, but the reverse is generally accepted. Obstruction may occur

owing to the very bulk of the cysts, or an intussusception or volvulus be precipitated by their presence.

X-ray Studies.—Characteristic radiological patterns have been described, and preoperative diagnosis has on occasion been made correctly by virtue of the *x*-ray appearance. Certainly *x*-ray studies offer the most useful diagnostic aid (Marshak *et al.*, 1956). Films of the abdomen in the erect position may demonstrate grape-like clusters of air shadows, the walls of the bowel being delineated by a double contour line (Paris, 1955). In colonic involvement, and in the absence of complete obstruction as occurred in our case, *x*-ray films after a barium enema may reveal the gas cysts as discrete lucent areas, indenting the regular contour of the bowel as a series of filling defects of varying sizes. Differentiation between gas cysts and diffuse polyposis may be difficult, however. The occasional occurrence of pneumoperitoneum has already been commented upon.

We thank Mr. T. M. Hennebry and Dr. J. F. Heggie for permission to report this case.

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Carcinoma of the Colon in a Child

Hoerner (1958) was able to collect 73 cases of carcinoma of the colon and 189 of carcinoma of the rectum occurring in subjects under 20 years of age and published between 1865 and 1958. Since then a case of carcinoma of the colon has been reported by Kern and White (1958) and three cases were added by Salem and Postlethwait (1960). Carcinoma of the colon may also occur in children in association with ulcerative colitis (Wilcox and Beattie, 1956). Compared with other neoplasms occurring in children, carcinoma of the colon is rare, there being no cases of this disease in a series of 965 children under 15 years with tumours quoted by Saner (1946).

CASE REPORT

A girl aged 13 years and 10 months, with no family history of intestinal disease, was first seen on November 23, 1959. In late 1957 she had started to complain of non-specific abdominal pain which recurred at intervals of about two to three months and lasted for a day or two at a time. In March, 1959, she began to have shooting pains in both groins which became worse, occurring about 10 times in each 24 hours by the time she was seen. Her mother thought she had lost weight. Her bowels had been normal; her appetite was poor, but she had had no nausea or vomiting. Menstruation had not begun, and her mother said that her two sisters had had similar troubles at puberty. On examination she weighed 4 st. 10½ lb. (30.3 kg.). No abnormal physical signs were found, but it was noted that no secondary sex characters had appeared. An E.S.R. was 12 mm. in one hour (Westergren).

During the next month she vomited three times, and the pain became localized to the umbilical region, slightly more severe, and more colicky in nature. Her bowels remained normal.

On December 24 she was admitted to hospital with increasingly severe colic. She had passed four loose motions on the day of admission. No definitely abnormal signs were found and her symptoms rapidly settled over the next two days. She had lost 2 lb. (0.9 kg.) in weight since her first attendance. An E.S.R. was 7 mm. in one hour (Westergren); Hb, 97%; W.B.C., 7,200/c.mm. The stool contained no pathogens or blood.

Her progress was followed as an out-patient during January, 1960, her weight continuing to fall. Her pain was less severe and she said she had dysuria. Guarding in the left hypochondrium was found. An intravenous pyelogram and urine examination were negative. At the beginning of February she complained of diarrhoea twice daily and said that her motions were occasionally streaked with blood. Her colic was again becoming worse and her abdomen had become slightly distended. She was readmitted on February 8.

Physical Findings.—She was a thin, wasted child weighing 4 st. 0 lb. 3 oz. (25.5 kg.), with follicular hyperkeratosis and no signs of puberty. The pulse rate was 80, and blood-pressure 110/70. She was tender in the left iliac fossa, but no mass was felt. Her abdomen was slightly distended with gas.

Investigations.—Hb, 93% (Haldane); W.B.C., 4,500/c.mm.; E.S.R., 11 mm./hour. Stool: occult blood present, no tubercle bacilli, fat excretion 2 g. a day. A sigmoidoscopy was reported on as being normal to 15 cm. A barium-enema examination (Fig. 1) showed a narrowed segment in the mid-descending colon extending almost to the splenic flexure. A diagnosis of Crohn's disease was suggested by the radiologist. A barium meal disclosed no abnormalities but caused an episode of acute intestinal obstruction lasting 24 hours.

Course and Treatment.—She contracted chicken-pox on February 30. On March 31 a laparotomy was performed

FIG. 1.—Barium enema showed a narrowed segment in the mid-descending colon extending almost to the splenic flexure.

(Mr. J. M. Pullan) and a hard knobbly mass was found replacing the descending colon. The omentum and peritoneum contained many small secondary deposits. A side-to-side by-pass anastomosis was performed between the transverse and sigmoid colon. A biopsy specimen showed a poorly differentiated mucus-secreting adenocarcinoma in which a "signet-ring" pattern predominated (Fig. 2). She was able to go home for two weeks only, and died on July 6, 1960.

Post-mortem Examination (Dr. H. Spencer).—Six inches (15 cm.) of the descending colon was found to be infiltrated with tumour. The ileum was distended to a point 2 ft. (30 cm.) above its termination, where it became partially obstructed through adhesion to a mass of carcinoma on the outer wall of the pelvic colon. A mass of secondary deposits filled the pelvis. There were numerous deposits in the peritoneum, matting the coils of small intestine. Several nodules of tumour were found in the liver capsule, but there were none in the parenchyma. No secondary deposits were found elsewhere.

COMMENT

The differences in symptoms and signs between neoplasms of the colon in adults and those in children are few, though the latter present more often with intestinal obstruction. Johnston (1947) estimated that at least 70% of cases in children present in this way. This is probably because in children not only is the progression of the disease more rapid (Salem and Postlethwait, 1960) but the diagnosis is more likely to be missed than in adults, owing to the rarity of this condition in the young. For example, a boy aged 15 years (Williams, 1954) was thought to have mesenteric adenitis, and after an appendicectomy had two further operations for colic in which adhesions were divided. Only at a fourth operation, six months after the first, was a carcinoma of the splenic flexure found.

The youngest case of carcinoma so far reported in an otherwise normal child is that of Kern and White (1958), whose patient was a girl of 9 months with a mucus-secreting adenocarcinoma of the transverse and descending colon. (Ahlfeld (1880) had previously described a stillborn monster with carcinoma of the colon.) Clar (1885) recorded a case of carcinoma of the colon in a 3-year-old boy, and from this age onwards the frequency of the disease increases progressively. In Johnston's (1947) series there were three patients aged under 5 years, eight aged 6 to 10 years, and 34 aged 11 to 15 years. The maximum incidence is reached at 49 to 65 years (Willis, 1953). The site distribution is the same as in adults (Johnston, 1947).

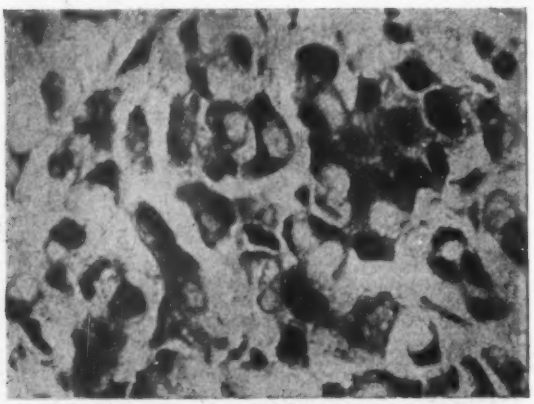

FIG. 2.—Photomicrograph (×550) showing a poorly differentiated mucus-secreting adenocarcinoma in which a "signet-ring" pattern predominated.

It has been estimated that 20% of all cases of rectal bleeding in children under 13 years is due to polyps (Mallam and Thomson, 1959); nevertheless, intestinal polyps, whether congenital or sporadic, do not seem to be frequent precursors of carcinoma of the colon in children. There were no cases of carcinoma of the colon in Mallam and Thomson's (1959) series of 183 children under the age of 13 years with polyps. Three children had a family history of polyposis. Kerr (1948) found malignant change in 2 out of 100 children with polyps, the younger being 12 years of age. Neither of these had a family history of polyposis.

Wilcox and Beattie (1956) described a case of carcinoma of the colon in a child with ulcerative colitis and cited four other proved and two presumptive cases from the literature. These patients were aged 11 to 15 years and had had bowel symptoms for between six and nine years.

Carcinoma of the colon in children shows one striking difference from that of adults, in that 50% of children with this disease have mucus-secreting growths, while these occur in only 5% of adult cases (Hoerner, 1958).

The prognosis is very bad, only one patient having survived for eight years after operation (Hoerner, 1958) and two others for seven (Scholefield, 1946) and four (Webster, 1938) years respectively.

In the case here reported symptoms referable to the abdomen were present for two and a half years before the diagnosis was made. It is presented to draw attention to a disease in which the prognosis might be improved by the wider recognition of its occurrence in childhood.

I thank Dr. D. G. Cottom (under whose care the patient was admitted) and Mr. J. M. Pullan for permission to publish this case; Dr. J. L. Pinniger for helpful criticism and advice; Dr. H. Spencer for the report of the post-mortem examination; and the photographic departments of St. Thomas's Hospital and the Medical School for the photographs.

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The number of patients given transfusion and the amount of blood used have risen steadily since the war. To keep pace the National Blood Transfusion Service has had to expand and must continue to do so. At the end of 1960 the number of enrolled donors stood at 853,753: during that year 1,024,141 blood donations were given—equivalent to two donations every minute of every hour, day and night. This is the first time that donations have exceeded the million mark.

Reviews

CHOOSING TO BE A DOCTOR

The Choice of a Medical Career. Essays on the Fields of Medicine. Edited by Joseph Garland, M.D., Sc.D.(Hon.), and Joseph Stokes III, M.D. (Pp. 231+x. 40s.) Philadelphia, Montreal: J. B. Lippincott Company. London: Pitman Medical Publishing Co. Ltd. 1961.

Parents are well aware of the difficulty of helping their children to choose a career. Trained advisers at the schools and appointments boards at the universities go some way towards remedying this difficulty, but there remain large tracts of ignorance. Moreover, it is no longer possible merely to recite, "army, navy, law, medicine, divinity, art." Each profession has become diversified as the result of specialization of knowledge, and this book on the choice of a medical career contains an account of a score of different careers in medicine, described by different authors. Each of them is proud of his special field of work and happy to be in it. Stokes, writing on paediatrics, speaks of the joy derived from the hopefulness inherent in the young, while Rusk, working at the other extreme of life, speaks of the glow of inner satisfaction from helping his fellow men to live rich and full lives despite their physical disabilities.

The book is well edited, and with one or two exceptions the authors do not romance too much about their task or dig too deep into its history. They are factual about the training requirements and the opportunities and interests of the work, and they try to forecast the prospects of their specialty. The articles on general practice, paediatrics, and psychiatry are especially interesting because of this projection into the future. The last article is overlong and repetitive and marred by occasional jargon such as "normative emotional crises" and "the parental generativity of the seasoned clinician"; but it stresses and demonstrates the importance of establishing departments of psychiatry within the teaching hospitals, since it is only in this way that the student can become properly aware that psychiatry offers a career he himself may wish to choose. One of the merits of an optional period in the final year in medicine is that it allows the student, while his future is still uncommitted, to learn a little more of a specialty to which he may have been attracted by an inspiring teacher or as the result of mere chance.

There are some interesting sidelights on American medicine. Premedical students are considered to be the most highly motivated group in the student body, but the altruistic and philanthropic aspects of love of mankind are said to be markedly lacking among them. In 1960 the National Institutes of Health had a budget of over $280m., more than $200m. of which was assigned to research projects or training programmes in universities and teaching hospitals. Since 1946 large sums of money have been allocated to psychiatry, and this has been the most effective force in the growth and development of psychiatry in the United States in the past 14 years.

L. J. WITTS.

ON CATARRHAL CHILDREN

The Catarrhal Child. By John Fry, M.D.(Lond.), F.R.C.S. (Eng.). (Pp. 139+viii. 25s.) London: Butterworths. 1961.

The schoolboy answering an examination question about the meaning of certain words had to scratch his head for a minute over "catarrh," and then he wrote: "A catarrh is a musical instrument, especially in Spain." Some of us, even after many years in paediatrics, have to confess that we are almost as puzzled as the schoolboy was about catarrh—especially regarding its causes and treatment. We all suffer with it from time to time and we have to treat many other sufferers, and really we ought to have put a knot in our overworked handkerchiefs to remind us that we should make a more determined effort to lay bare the secrets of this plague.

All the more credit, then, to Dr. John Fry, who has faced up to the problem in his general practice in suburban London and has written this small but important book in which he tells us what he found, what he did about it, and what his results were. There were about 750 children under the age of 10 years, and his observations cover the 10-year period 1949 to 1958. Careful records were kept of each child who developed any kind of respiratory catarrh, and each year nearly 60% of the children were afflicted at least once. Fry groups them into broad clinical categories ("coughs and colds," "acute chest infections," "the wheezy child," "acute otitis media," and "acute throat infections"), and he summarizes his findings in each group and the treatment he used. There is a good deal of detailed information which will be found easy to follow, interesting, and stimulating by all doctors who have to deal with these cases, and also by medical administrators. Reference is also made to the reports of other workers.

Chapters 8 and 9 are of special interest, because they deal with the vexed questions of tonsils and adenoids and the use of antibiotics for respiratory catarrh. Dr. Fry's common-sense approach, based upon sane reasoning and his own clinical experience, is like a breath of fresh air blowing into a fuggy room, and I ask all general practitioners and hospital doctors to read and ponder what he says, especially as he says it pointedly yet generously. There is a bias towards adopting a conservative attitude in treatment, but it is amply sustained by the author's own experience and his thoughtful weighing-up of available evidence presented by other workers.

The final chapter deals with general management, and I particularly want to stress the author's insistence upon the need for establishing good personal relations between the doctor, the child, and the mother.

This book is to be commended wholeheartedly as a thoroughly rational and valuable contribution to a controversial subject of national importance. And when you read it you will quickly realize that you are being given a view of clinical medicine at its best.

There are a few slips (pp. 104, 109, and 130), but only one that came as a shock—the incorrect spelling of Sir Robert Hutchison's name on page 6.

N. B. CAPON.

RED-CELL PHYSIOLOGY AND PATHOLOGY

The Red Cell. By T. A. J. Prankerd, M.D. (Pp. 184, illustrated; 32s. 6d.) Oxford: Blackwell Scientific Publications. 1961.

During the last two decades the concept of the red cell as an inert sac containing haemoglobin has changed to that of a cell with a complicated structural membrane and an active metabolism of its own. Dr. Prankerd has set out to assemble the available knowledge about the physical structure of the red cell and about the

biochemical aspects which have so far been elucidated The book is in two parts. The first deals with the physiological chemistry of the cell under the chapter headings of morphology and ageing, molecular structure, permeability, metabolism, haemolytic mechanisms, and blood storage. The second part is concerned with the chemical pathology under similar headings. The aim of the book is to provide a meeting-ground for those working on the basic problems of the biochemistry and physiology of the red cell on the one hand and the clinical haematologist on the other, and this has been admirably achieved. All aspects are discussed in considerable detail and there is an extensive bibliography.

There are, unfortunately, a number of errors, which include misprints (such as metabisulphate instead of metabisulphite), the inclusion of references in the text which have been omitted in the bibliography, and an incorrect formula on p. 7. This formula is supposed to give an expression for the determination of red cell survival from ^{51}Cr data, but it is meaningless as it stands. It does, however, resemble the formula used by others for converting ^{51}Cr survival figures on any particular day into the true red-cell survival. Apart from this, the book is excellently written. All research workers and clinical haematologists will find the critical presentation of so many aspects of red-cell physiology and pathology most valuable.

N. C. HUGHES JONES.

HORMONES IN BLOOD

Hormones in Human Plasma. Nature and Transport. Edited by Harry N. Antoniades, Ph.D. Thirty-three contributors. Foreword by George W. Thorn, M.D., LL.D., S.D.(Hon.). (Pp. 667+xvii. £9.) London: J. and A. Churchill Ltd. 1960.

Advances in hormone chemistry and in the elucidation of endocrine functions have been rapid, but they have not been matched by similarly precise information on the release, transport, and metabolism of hormones. Work on all these problems requires accurate, specific, and sensitive methods for the estimation of hormones in blood. Biological assays have to be used in most instances, and their evaluation presents many difficulties. Hence the pioneer Ciba Symposium on Hormones in Blood in 1957 (which surprisingly enough is not mentioned in either the foreword or the preface of the book under review), and hence the present volume, which is a valiant attempt by 33 specialists (30 from American institutions) to present fragmentary and often confusing results in a systematic way. Much space is devoted to the critical discussion of assay methods, and this has been done in a stimulating manner. For example, J. E. Crigler (pp. 203–205) shows that the sensitivity of methods for the estimation of thyrotropic hormone (T.S.H.) described during the last five years varies from 10 to 3,000 micro-units, and P. L. Munson (p. 185) points out that tests for linearity and parallelism are not available for the much-practised assays for corticotrophin (A.C.T.H.). Other useful features are a chapter by J. L. Oncley on plasma and plasma fractionation, and a section by Antoniades, Doughaday, and Slaunwhite on the protein binding of steroid hormones which collects much widely dispersed material. It could profitably have been longer.

The book is well written and produced. There are few misprints, though Able for Abel on the very first page is disturbing. It will be of considerable value to endocrinologists and clinical pathologists, and should also appeal to the wider medical public, if only to show the unreliability of many values for hormone concentrations in plasma reported for a variety of pathological states.

H. HELLER.

FOETAL ELECTROCARDIOGRAPHY

Fetal Electrocardiography. The Electrical Activity of the Fetal Heart. By Saul David Larks, B.S.E.E., M.S.(E.E.), Ph.D. (Pp. 109+xiii; illustrated. 52s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1961.

Dr. Larks believes that foetal electrocardiography has much to offer as a diagnostic aid during pregnancy, and in this book he aims to show that it can be of value not only in problems of clinical management but also as a research tool.

The author describes the technique of foetal electrocardiography, in which the essential factor is an electrocardiograph capable of 100 times greater amplification than the standard electrocardiograph. This is made necessary by the fact that the amplitude of the foetal R wave is only of the order of 10 to 100 microvolts at the maternal body wall. The problems of elimination of interference in such a sensitive instrument are overcome by the use of high-gain balanced amplifiers, with, in addition, a device for limiting frequencies above 50 cycles. The electrode positions recommended are on the abdominal wall and on the back, and the leads recorded are bipolar leads. There are four basic twin electrode positions: (1) above the umbilicus and above the symphysis pubis, (2) paired electrodes placed transversely across the abdomen on a horizontal line below the umbilicus, (3) above the umbilicus and above the coccyx, and (4) below the umbilicus and above the coccyx. With these electrode positions satisfactory foetal electrocardiograms can be obtained even in the presence of considerable obesity and of hydramnios. The disturbance to the mother in recording the foetal electrocardiogram is negligible.

A number of case reports are cited where management of a patient with threatened abortion was greatly helped by the certain knowledge, obtained from the foetal electrocardiogram, that the foetus was still alive though the foetal heart sounds were not audible. Foetal distress can also be readily recognized in the foetal electrocardiogram in cases where the foetal heart sounds are poorly heard, and the progress of the foetus can be watched conveniently on serial tracings. Since twin pregnancies can be recognized in the foetal electrocardiogram by the presence of two independent foetal R waves with independent rhythms, this method may avoid the necessity of radiography when the diagnosis is uncertain.

As examples of research fields where the technique might be of value, Dr. Larks mentions the possibility of making the diagnosis of congenital heart disease *in utero* by the recognition of an abnormal QRS complex in the foetal electrocardiogram. He also stresses its potential value in assessing the dangers to the foetus in certain forms of maternal treatment, such as instrumentation and the administration of nitrous oxide.

A feature of the book is the useful and lucid introduction to bio-electric phenomena at the beginning, and also the high quality of the illustrations.

J. P. D. MOUNSEY.

SELECTING STUDENTS

The Chosen Few. An Examination of Some Aspects of University Selection in Britain. By W. D. Furneaux, B.Sc. (Pp. 245+xxvi. 25s.) London, New York, Toronto: Oxford University Press, for the Nuffield Foundation. 1961.

In 1948 the Nuffield Foundation allocated money for a 10-year investigation into the problems of selecting students for university education. This is the first of two volumes reporting that work.

As a matter of policy it had been decided not to publish until the whole survey was complete. For the second volume, in which the major results of the psychometric testing programme are promised, this will probably prove an advantage. This first volume is a general survey of the social and educational background as it was when the research was under way in the fifties; hence it is a bit dated. Much of the discussion of early-leaving from grammar schools has been rendered less relevant by recent social trends. Arguments for rationalizing methods of applying to universities which would have been strikingly original five years ago are no longer novel. Nevertheless, those interested in problems of students must not let themselves be put off by this; they will find the book a careful, painstaking work and one which will form an essential introduction to the most important original work to be reported in the second volume.

Though the importance of this kind of educational research is being increasingly realized, the difficulties of the worker who would study British universities are still great. What frustration is buried behind Mr. Furneaux's reserved passage on p. 133: "It was originally hoped that representative samples of students could be studied from both the traditional and also from modern universities. Unfortunately, it did not prove to be possible to carry out work at either Oxford or Cambridge . . ."

NICOLAS MALLESON.

UKRAINIAN PHYSIOLOGY

Problems of the Physiology of the Processes of Fatigue and Recovery. Translated by M. Roublev. (Pp. 264. No price.) Kiev: Academy of Sciences of the Ukrainian S.S.R. 1958.

The 25 papers in this monograph are of considerable interest to neurophysiologists because they provide an important insight into the Ukrainian School of Physiology, its response to the stimulus of Pavlov and the leadership of G. V. Fol'bort.

These papers fall into two groups, original papers and reviews, the latter predominating. Some have no bibliography or references—in fact, are straight essays. Where references are given they tend to be in high percentage to Ukrainian papers; when to foreign papers the tendency is to restrict them to the classical papers from Claude Bernard to A. V. Hill. There are very few references to active work in the field of the paper, whether European or American. The opening paper by Fol'bort provides an excellent history of his training by Pavlov and of the rise of the Pavlovian school of neurology and neurophysiology. It illustrates, too, how the aim of justifying and applying a "Pavlovian" approach and interpretation of biology competes very successfully with alternative and perhaps less disinterested and more objective approaches.

The value of this monograph lies in its conspectus of Ukrainian physiology and it serves to emphasize the need for readier access to Russian original papers, together with a removal of language barriers.

A. ST. G. HUGGETT.

BOOKS RECEIVED

Review is not precluded by notice here of books recently received.

Proceedings of the Rudolf Virchow Medical Society in the City of New York. Volume XVIII, 1959. Edited by the Publication Committee: Hans E. Bejach, Ernst Bergmann, and George Schreiber. (Pp. 182; illustrated. 22 Swiss Fr.) Basel, Switzerland, and New York: S. Karger. 1959.

Roxburgh's Common Skin Diseases. Twelfth edition. Revised by Peter Borrie, M.A., M.D.Cantab., F.R.C.P.London. (Pp. 505+xxiii; illustrated. 50s.) London: H. K. Lewis and Co. Ltd. 1961.

No Time for Prejudice. A Story of the Integration of Negroes in Nursing in the United States. By Mabel Keaton Staupers, R.N. (Pp. 206+xiii. 34s. 6d.) New York and London: The Macmillan Company. 1961.

Chemical Ultrastructure in Living Tissues. By J. B. Finean, D.Sc. (Pp. 131+xii; illustrated. 48s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications Ltd. 1961.

Symptoms and Signs in Clinical Medicine. An Introduction to Medical Diagnosis. By E. Noble Chamberlain, M.D., M.Sc., F.R.C.P. Seventh edition. (Pp. 569+xi; illustrated. 45s.) Bristol: John Wright and Sons Ltd. 1961.

Cerebral Anoxia and the Electroencephalogram. The Proceedings of the Marseille Colloquium, sponsored by the Réunion Européene d'Information Eléctroencephalographique, and organized by Professor H. Gastaut and Dr. H. Fischgold. Edited by Henri Gastaut, M.D., and John Stirling Meyer, B.S., M.Sc., M.D., C.M. (Pp. 617+xiii; illustrated. £9 16s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications Ltd. 1961.

The Spinal Cord. Basic Aspects and Surgical Considerations. By George Austin. (Pp. 532+xiv; illustrated. £10 12s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications Ltd. 1961.

Advances in Oto-Rhino-Laryngology. Volumes 8–10. Seventh International Congress of Oto-Rhino-Laryngologists. Paris, 23–29 July, 1961. Edited by Professor Dr. E. Rüedi. (Vol. VIII, pp. 428+ix; illustrated. 48 Swiss Fr. Vol. IX, pp. 323+ix; illustrated. 26 Swiss Fr. Vol. X, pp. 233+x; illustrated. 26 Swiss Fr.) Basel and New York: S. Karger. 1961.

711 Medical Maxims. Volume II. By William S. Reveno, M.D. (Pp. 177+xi. 28s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications Ltd. 1961.

Glaucoma. Chemistry, Mechanisms and Therapy. By Sidney Lerman, M.D., C.M. (Pp. 111+xii; illustrated. 52s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications Ltd. 1961.

Hemoglobin and its Abnormalities. By Vernon M. Ingram, Ph.D. (Pp. 153+xiv; illustrated. 60s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications Ltd. 1961.

Tools of Biological Research. Third Series. Edited by Hedley J. B. Atkins, D.M., M.Ch., F.R.C.S.Eng., Hon.F.A.C.S. (Pp. 155+xii; illustrated. 37s. 6d.) Oxford: Blackwell Scientific Publications Ltd. 1961.

Diseases of the Intervertebral Disc and its Surrounding Tissues. By Reuben Radinovitch, B.A., M.Sc., M.D. (Pp. 152+xii; illustrated. 68s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications, Ltd. 1961.

Cancer Chemotherapy. Prepared by the Staff of the University of Texas M. D. Anderson Hospital and Tumor Institute, Texas Medical Center, Houston, Texas. Under the direction of R. Lee Clark, jun., M.D., D.Sc.(Hon.). (Pp. 253+xii; illustrated. 84s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications Ltd. 1961.

Hypokinetic Disease. Diseases Produced by Lack of Exercise. By Hans Kraus, M.D., and Wilhelm Raab, M.D. (Pp. 193+ix; illustrated. 60s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications Ltd. 1961.

BRITISH MEDICAL JOURNAL
LONDON
SATURDAY SEPTEMBER 16 1961

THE CONTRACEPTIVE PILL

Ovulation can be stopped by administering oestrogens, androgens, or progestogens. For various reasons the first two are unsuitable to use for contraception, while the hormone progesterone is inactive when taken orally. But a contraceptive pill became possible when biochemists synthesized substances which, remaining active when taken by mouth, have a progesterone-like effect in stopping ovulation. Among the several tested for this purpose the most suitable was norethynodrel. It has slight oestrogenic activity, which helps the inhibition of ovulation, and this activity is enhanced in the contraceptive pill at present marketed ("conovid") by the addition of a small amount of ethynyl-oestradiol-3-methyl ether. The conovid pill contains 0.075 mg. (1.5%) of this substance and 5 mg. of norethynodrel. A pill of the same composition is also marketed under the name "enavid" (5 mg. or 10 mg.) for the treatment of patients with hormonal disturbances. The mechanism by which these drugs inhibit ovulation is not precisely understood, but they are believed to block the synthesis of gonadotrophic hormones in the anterior pituitary.

A much larger collection of data than has yet been gathered will be needed before a clear assessment of the efficacy and safety of contraception by this method becomes possible. Meanwhile patients are arriving in their doctors' surgeries and asking for information about these pills and prescriptions for them. Perhaps the least difficult question to answer is on efficacy. The data on this were reviewed recently under "To-day's Drugs" in this journal,[1] and they show that as a contraceptive the pill is effective when taken as instructed. Side-effects in up to about one-third[2] of those who start taking conovid may be expected, but usually disappear after a few cycles of administration. They include nausea, headache, dizziness, breast engorgement, and weight gain. "Break-through bleeding" can occur and cause the patient anxiety. The advice of the Family Planning Association's Medical Advisory Council[2] is to "ignore spotting but to stop taking the pills if frank bleeding occurs and to start treatment again on the fifth day as if this had been a normal [menstrual] bleeding."

A far more worrying problem for the medical adviser concerns the safety of these pills if taken over many years, and it has aroused some discussion in the columns of this journal as well as in the U.S.A.[3] Prolonged interference with such a primitive biological mechanism as ovulation would seem to demand the most careful supervision. As the pills (under Schedule 4, Part B, of the Poisons Rules) are obtainable only on a medical prescription, the opportunity for it exists. But in the present state of knowledge, based first on animal experiments and later on clinical trials, no certain answer seems possible to several important questions. One is whether the endocrine system will become permanently impaired and perhaps fertility reduced or destroyed. The Family Planning Association's Medical Advisory Council[2] stated that "in animals when pituitary activity is inhibited its effects are all entirely reversible, with the exception that, if oestrogen is administered continuously to a rat for two-thirds of its life, pituitary adenoma may appear." On the other hand, after more than five years' clinical trials with norethynodrel the F.P.A. reported that "so far there does not appear to be any long-term effect on the ovary or pituitary." Another question is whether these substances could be carcinogenic, and the F.P.A.'s discussion of this is reassuring. In short, there seems nothing to add yet to the conclusion set out earlier in this journal[1]: "Though the likelihood of these oral contraceptives being carcinogenic is probably extremely remote, and though fears that they might cause congenital defects in babies born subsequently are probably groundless, it still remains to be shown that the suppression of ovulation over long periods is harmless to the endocrine system and to ovario-uterine relations."

Finally a problem of a rather different kind is troubling general practitioners and was recently discussed in the General Medical Services Committee.[4] Since patients can get contraceptive pills only on medical prescriptions they are asking their doctors to prescribe them under the Health Service on Form E.C.10. A doctor is at liberty to do this, but, if he does, the Ministry of Health may ask him to justify the cost of it—and his explanation might not be accepted. At the G.M.S. Committee's discussion Dr. A. N. Mathias said that the prescription of contraceptive pills in the N.H.S. was "a matter of public policy on which the Minister must make up his mind." But the individual doctor in charge of the individual patient in the meantime

[1] *Brit. med. J.*, 1961, **1**, 667.
[2] Ibid., 1960, **2**, 380.
[3] Tyler, E. T., *J. Amer. med. Ass.*, 1961, **175**, 225.
[4] *Brit. med. J. Suppl.*, 1961, **2**, 135.

is in a dilemma. If he is convinced that such a prescription is in the interest of his patient's health is he justified in not prescribing it on Form E.C.10? As the planned spacing of families is now advocated by responsible public and medical opinion the demand by the public for contraceptive pills is bound to grow. In the present state of knowledge of the efficacy and potential hazards of the pill it would obviously be wise to hasten slowly in its distribution to the public.

THE RIDDLE OF CEREBRAL INFARCTION

Studies on the diagnosis and management of cases of cerebrovascular disease are proceeding apace owing to the possibility of giving successful treatment by anticoagulants and arterial surgery. Formerly much attention was directed to disease of the intracranial arteries, and because of the view, expressed by Cohnheim[1] among others, that cerebral arteries must be regarded as end arteries the delineation of syndromes on a topographical basis became fashionable. Clinical pictures of precise symptomatology were attributed to lesions of the posterior inferior cerebellar artery, the middle cerebral, the posterior cerebral, portions of the anterior cerebral before and after the origin of Heubner's branch, and so on in the most delicate refinement of doctrinaire anatomy.

Dissenters and nonconformists arose but were largely ignored, and Hughlings Jackson[2] believed that cerebral softening was always due to local arterial disease. In 1927 C. Foix, P. Hillemand, and J. Ley,[3] who had previously associated themselves eponymously with local arterial syndromes, were somewhat surprised to find in a study of cerebral infarction how often the local arteries were normal. For a time the magical phenomenon of vasospasm was adduced to explain such disorders as well as the transient motor and sensory disturbances which are now known to precede carotid occlusion.

Clues to the real state of affairs could already be discerned, and J. R. Hunt in 1914[4] had already drawn attention to the fact that obstruction in the carotids might combine with heart disease to produce a picture of intermittent cerebral claudication. G. T. J. Hultquist[5] in 1942 found carotid occlusion in 2.9% of unselected necropsies, and M. Fisher[6] and K. C. Samuel[7] drew attention to the frequency of stenosis and occlusion of the carotid arteries. Subsequently much has been written on the clinical and pathological factors of obstructions in the internal carotid arteries. E. C. Hutchinson and P. O. Yates[8] extended these ideas to the extracranial portions of the vertebral arteries, and showed the importance of viewing the problem of the cerebral circulation in terms of the total effect of the four arteries of supply. Their earlier work on carotico-vertebral stenosis has now been expanded into a monograph[9] published by the Medical Research Council and contains a detailed account of the importance of the role of stenosis of the extracranial arteries in the production of cerebral infarction. They found that of 35 patients dying of cerebral infarction 22 showed serious narrowing or thrombosis of the extracranial cerebral arteries and that only in 15 were the relevant intracranial arteries occluded. It is obvious too that there is much greater evidence of anastomoses than was previously thought. Due weight is given to the contributory factors of general diseases such as anaemia and hypotension resulting from heart disease, and clearly intracranial arterial disease may co-exist with disease of the extracranial structures.

This clarification of the anatomical and pathological issues leads to a reconsideration of the therapeutic possibilities. If the cerebral disorder were always a manifestation of generalized peripheral arterial disease, then therapy would have to be directed to the biochemical means of correcting arterial degeneration or of reducing the danger of the final thrombosis. This approach presents difficulties, some of which were considered earlier this year in a leading article[10] on the present doubtful position of anticoagulant therapy in cerebrovascular disease. But if there are a significant number of cases in which the prime disorder consists of a relatively localized lesion of major arteries in the neck, accessible to the surgeon, the idea of operative relief becomes at least superficially attractive.

Unfortunately the problems confronting the surgeon are also great. Precise anatomical diagnosis is itself singularly difficult, since the demonstration of an obvious stenosis or occlusion in the proximal portion of the carotid can never rule out the possibility of more widespread disease of the distal cerebral arteries. Indeed, dramatic improvement after operation is rare if total occlusion has occurred, because the damaged cerebral tissue is apt to be incapable of responding satisfactorily to the restored

[1] Cohnheim, J., *Untersuchungen über die embollschen Processe*, 1872. Hirschwald, Berlin.
[2] Jackson, J. H., *Lancet*, 1875, **2**, 335.
[3] Foix, C., Hillemand, P., and Ley, J., *Bull. Soc. Méd. Paris*, 1927, **51**, 189.
[4] Hunt, J. R., *Amer. J. med. Sci.*, 1914, **147**, 704.
[5] Hultquist, G. T. J., *Uber Thrombose und Embolie der Arteria Carotis*, 1942. Stockholm.
[6] Fisher, M., *Arch. Neurol. Psychiat. Chicago*, 1954, **72**, 187.
[7] Samuel, K. C., *J. Path. Bact.*, 1956, **71**, 391.
[8] Hutchinson, E. C., and Yates, P. O., *Lancet*, 1957, **1**, 2.
[9] Yates, P. O., and Hutchinson, E. C., *M.R.C. Monograph, Cerebral Infarction*, 1961.
[10] *Brit. med. J.*, 1961, **1**, 1094.
[11] Edwards, C. H., Gordon, N. S., and Rob, C., *Quart. J. Med.*, 1960, **29**, 67.

blood flow even if there is no local arterial occlusion. C. H. Edwards and colleagues[11] concluded that "the patients most likely to benefit from operation are those with a partial obstruction of the artery whose history is of a 'stuttering' onset of symptoms." They thought this might be because the diagnosis was made before severe and permanent neurological disability had developed. But they found the worst results were in patients with partial arterial block and a gradual onset of symptoms. The explanation they suggest is that in these cases there may be structural lesions other than mere arterial narrowing. In some cases, however, the restoration of an occluded channel—even if it does not produce improvement in the clinical picture—is probably a useful prophylactic measure against further infarctions in territories supplied by the other cerebral arteries, though against this must be set the danger of embolism during or after operation.

IMMUNIZATION SCHEDULES

For a long time doctors (and parents) have been seeking authoritative guidance on the immunization of children. When a speaker at the Annual Representative Meeting two years ago moved that the Council of the B.M.A. be instructed to produce model immunization schemes suitable for children and adults he was told that the Standing Medical Advisory Committee had such a scheme in an advanced stage of preparation.[1] This scheme has now at last seen the light of day in the form of a memorandum from the Ministry of Health (see p. 763). In the intervening years doctors have not been without useful advice, for a good start towards the drawing up of immunization schedules was made in May, 1959, when a symposium on immunization in childhood was sponsored by the Wellcome Foundation.[2] Of the two recommended schedules then put forward, Schedule B has been widely accepted both in Britain and abroad, and last year the Thirteenth World Health Assembly[3] approved a schedule (for areas with adequate public health medical services) which was very similar to Schedule B. General practitioners, medical officers of health, and all concerned with immunization in Britain will be grateful for the authoritative lead now given by the Ministry of Health. The selection of the more efficient, or more practicable, of the alternative schedules offered is left to the individual doctor, but the notes provided will help him in his choice.

It is evident from the schedules that combined vaccines have now replaced single antigens. This is a step towards the eventual banishment of the fear of "provocation" poliomyelitis—a threat which has hung over the heads of general practitioners and clinic medical officers since the report[4] from the Medical Research Council in 1956. The Ministry's memorandum discusses the risk, which must now be very slight, since in the area of the London County Council over half a million injections of combined prophylactics (without alum) have been given in the last few years, and only one (dubious) case of paralytic poliomyelitis occurred within 28 days of an injection.

Of the alternative schedules P and Q, most doctors are likely to choose schedule P, which is very similar to the widely used Schedule B of the Wellcome Symposium. In Schedule Q immunization does not start until the age of 6 months, two reasons being given for this: first, antigens may not provoke a maximum response in young infants, in whom also maternally transmitted antibodies may interfere with the response, and, secondly, the giving of protection against poliomyelitis before the administration of combined vaccines may reduce the risk of "provocation" poliomyelitis. Many immunologists would not accept these arguments as valid. While it is true that infants may not respond fully to all antigens administered in the early months of life, any deficiency can be made good by the reinforcing dose given around the age of 18 months. It has also been suggested that failure of the antibody-producing mechanism to respond in young infants may sometimes be due to inferior antigens rather than to immaturity.[4] The risk of "provocation" poliomyelitis, as already said, is now very slight.

Two objections may be put forward against Schedule Q. First, there is no attempt to protect the young infant against whooping-cough, and, secondly, the attendances at immunization clinics would probably fall if mothers had to wait until their babies were 6 months old. Most medical officers of clinics would agree with the motto, "Catch 'em young." It is the mother of a baby 4 to 6 weeks old, grateful for comprehensive antenatal and post-natal care, who is most likely to co-operate in the primary immunization of her baby—just as it is the noisy and boisterous child of 6 to 8 months who is going to be more awkward to inoculate. In the first month or so after birth there is the happy combination of a keen and responsive mother with a disinterested and sleepy infant. Schedule Q, however, is of value when children are presented for the first time for immunization at the age of 6 months and upwards, and recalls the schedules for "late starters" proposed by I. Taylor.[6]

In both Schedules P and Q the age for smallpox vaccination is given as 4 to 5 months: here, apparently, the Ministry has decided against the small minority of doctors who believe that there is less risk of post-vaccinal complications after the age of 1 year. A minor criticism of the schedules is that the triple vaccine is described as "diphtheria/pertussis/tetanus vaccine" (which would be DPT/Vac), whereas the official *B.P.* preparation is "diphtheria, tetanus, and pertussis vaccine (DTP/Vac)—a small point, but perhaps one which could lead to confusion. What is most satisfactory, however, is that these nationally recommended schedules for immunization in childhood should immediately lead to more uniformity of practice in this vital sphere of public health.

[1] *Brit. med. J. Suppl.*, 1959, 2, 59.
[2] *Proceedings of a Symposium on Immunization in Childhood*, 1960. E. and S. Livingstone, Edinburgh. See also *Brit. med. J.*, 1959, 1, 1342.
[3] *The Role of Immunization in Communicable Disease Control*, 1961. World Health Organization, Geneva.
[4] *Lancet*, 1956, 2, 1223.
[5] Barr, Mollie, *et al.*, ibid., 1952, 2, 803.
[6] Taylor, I., *Brit. med. J.*, 1959, 2, 884.

SPONTANEOUS PREMATURE RUPTURE OF THE MEMBRANES

A problem which from time to time confronts the obstetrician, whether specialist or general practitioner, is posed by the woman whose membranes rupture spontaneously without labour having started or starting soon after. The incidence of this mishap varies from a little more than 7%[1] to a little less than 16%,[2] and in the U.S.A. it has been noted to be more common in women of the lowest socio-economic classes. The membranes may rupture as early as the 15th week of pregnancy,[3] but only about 20% of cases occur before the 36th week, and prolapse of the cord is a surprisingly rare complication. As to the prognosis for the baby, it had been noted that the longer the interval between the rupture and the onset of labour the greater the foetal loss,[4] but N. J. Eastman showed that the outcome depended mainly on the maturity of the baby as judged by its birth weight.[5] In mature babies the latent period was the major factor, inasmuch as the perinatal mortality was quadrupled from 1.7% to 6.8% when the onset of labour was more than 48 hours after rupture of the membranes. But when the foetus was premature the mortality rate was largely determined by the degree of prematurity. Even if the premature baby survived delivery it might succumb to infection, notably of the lungs, acquired in utero. It seems logical, therefore, when the membranes rupture prematurely, to expedite the onset of labour if the baby is mature, but to avoid active measures if the foetus is judged premature.[6] If the patient is booked for home confinement, and the foetus is adjudged mature, the mother may be allowed to remain at home for up to 24 hours to see whether labour supervenes, as in four cases out of five it will within that time. But if labour does not start by then, the patient is transferred to hospital, where a pitocin drip may be effective. If, however, the baby is considered premature, the mother is at once removed to hospital so that all the facilities of the premature-baby unit are immediately available if required. If liquor ceases to drain and there is no evidence of infection, the mother may be allowed home after a few days.

Certain points, however, remain to be elucidated. First, the cause of spontaneous premature rupture of the membranes is not known. Its occurrence is unrelated to the tensile strength of the membranes,[7 8] and D. N. Danforth believes that the cause may lie in secretions and forces to which the membranes are subjected.[9] Secondly, there is as yet no certain method of averting threatened premature labour in these cases; in particular, progesterone[10] and relaxin[11 12] are ineffective. Thirdly, there are a few perplexing cases in which liquor continues to drain for weeks or even months. In this type of case, the pathology of which has been discussed by C. W. F. Burnett,[13] masterly inactivity is probably the best policy, but the incidence of foetal abnormality in such pregnancies is slightly higher than average. Finally, the place for antibiotic therapy is still uncertain except where there is clinical evidence of maternal infection. Otherwise antibiotics are not required while the patient is at home. In hospital the local flora soon invades the maternal genital tract[14]; nevertheless prophylactic antibiotics may be best withheld until labour starts, when they may be given for the benefit of the foetus. As about 25% of the neonatal mortality in the premature babies is due to infection,[1] it seems advisable to prescribe antibiotics routinely for the premature baby delivered after spontaneous premature rupture of the membranes.

[1] Lebherz, T. B., Boyce, C. R., and Huston, J. W., *Amer. J. Obstet. Gynec.*, 1961, **81**, 658.
[2] Flowers, C. E., *et al.*, ibid., 1958, **76**, 761.
[3] Ekvall, L. D., Wixted, W. G., and Dyer, I., ibid., 1961, **81**, 848.
[4] Embrey, M. P., *J. Obstet. Gynaec. Brit. Emp.*, 1953, **60**, 37.
[5] Eastman, N. J., *Williams' Obstetrics*, 11th ed., 1956, p. 423. New York.
[6] Bender, S., *Brit. med. J.*, 1959, **1**, 497.
[7] Embrey, M. P., *J. Obstet. Gynaec. Brit. Emp.*, 1954, **61**, 793.
[8] Danforth, D. N., ibid., 1956, **63**, 237.
[9] —— *Amer. J. Obstet. Gynec.*, 1961, **81**, 856.
[10] Fuchs, F., and Stakemann, G., ibid., 1960, **79**, 172.
[11] Israel, S. L., and Groeber, W. R., *Obstet. and Gynec.*, 1960, **15**, 2.
[12] Embrey, M. P., and Garrett, W. J., *J. Obstet. Gynaec. Brit. Emp.*, 1959, **66**, 594.
[13] Burnett, C. W. F., ibid., 1957, **64**, 79.
[14] Mengert, W. F., *Amer. J. Obstet. Gynec.*, 1961, **81**, 857.

A NEW CONCEPT OF PNEUMATOSIS INTESTINALIS

An important contribution to our knowledge of the aetiology of pneumatosis intestinalis has recently been made by W. S. Keyting and colleagues.[1] This disorder is characterized by gas-filled cystic spaces in the walls of the intestine and is sometimes known as pneumatosis cystoides intestinalis. A case is reported elsewhere in this issue (p. 747) by Mr. J. I. Burn and Dr. B. S. Jones.

For some time it has been known that the condition is apt to occur in association with organic disease of the gastrointestinal tract, especially peptic ulceration and pyloric obstruction. It has also followed sigmoidoscopy and biopsy of the sigmoid colon. L. G. Koss[2] found that about 60% of the cases were secondary to such mechanical disturbances of the gut. The remaining 40% were regarded as "primary" because no explanation for their occurrence was apparent. The possibility of gas-producing bacteria being responsible for these "primary" cases has been mooted but never convincingly established.

Keyting and his colleagues had their attention attracted to the condition by seeing within one month three examples in patients who all suffered from severe pulmonary disease but had no evidence of gastrointestinal disease other than the pneumatosis. They were further stimulated to inquiry by the report by H. P. Doub and J. J. Shea[3] of sixteen cases of pneumatosis intestinalis of which fifteen were associated with asthma and one with pulmonary fibrosis.

It had previously been shown by C. C. Macklin[4] that experimental rupture of lung alveoli was followed by air tracking along the pulmonary vessels to the lung root and mediastinum, whence it might travel along different routes, one of them leading to the retroperitoneal space. Keyting and his colleagues found that, when air was injected into the root of the left lung in thoracotomized dogs, it sometimes passed down the supporting tissues surrounding the aorta until it vanished through the diaphragm. Twenty-four hours later, plain *x*-ray films

[1] Keyting, W. S., McCarver, R. R., Kovarik, J. L., and Daywitt, A. L., *Radiology*, 1961, **76**, 733.
[2] Koss, L. G., *Arch. Path.*, 1952, **53**, 523.
[3] Doub, H. P., and Shea, J. J., *J. Amer. med. Ass.*, 1960, **172**, 1238.
[4] Macklin, C. C., *Arch. intern. Med.*, 1939, **64**, 913.

and barium-enema examinations showed the presence of pneumatosis affecting the left side of the colon. In experiments on the human cadaver it was found that air injected into the tissues immediately surrounding the origin of the inferior mesenteric artery would follow the course of this vessel to the wall of the left colon. The air then climbed subserosally over the colon and thereafter spread by dissection throughout the colon, with the production of many small cysts, some of which became confluent.

As a result of these findings Keyting and his colleagues contend that the classification of pneumatosis intestinalis into primary and secondary types should be abandoned. They believe that all examples of the condition are secondary to disease or damage elsewhere. In some cases the air originates in a lesion in the gastrointestinal tract which breaks the continuity of the mucosa, and in the remainder it originates in pulmonary alveolar rupture brought about by severe coughing. The fact that the composition of the "air" in the cystic spaces is variable, with nitrogen present in higher concentration than in atmospheric air, is readily explicable on the basis of differential rates of absorption of gases by the tissues.

MALE AND FEMALE

Like many things connected with astronomy the well-known symbols for male and female, ♂ and ♀, have a long and sometimes legendary history. In a scholarly note on them W. T. Stearn,[1] of the British Museum (Natural History), has recently sorted fact from fiction, and he rejects as a myth the idea prevalent to-day that ♂ represents the shield and spear of Mars, ♀ the hand-mirror of Venus. In brief, he accepts the conclusion of the French scholar Claude de Saumaise (1588–1653) that the symbols are derived from contractions in Greek script of the Greek names of the planets. How they came into use is a strange story.

In the early days of astronomy the idea grew up that the heavenly bodies had some special relationship with earthly things and events. To a limited extent the truth of this is evident, as in the influence of the sun on the growth of plants and the moon on the tides. When elaborated and systematized these beliefs formed the subject of astrology, which in turn was linked with alchemy, and under the impact of these ideas men came to identify certain metals with certain planets. As a convenient short-hand in alchemical works they would denote the metals by the planetary symbols, thereby anticipating the chemical notation devised by the Swedish chemist and professor of medicine J. J. Berzelius (1779–1848). He gave us the symbols we use to-day, so that we write Fe instead of ♂ for iron and Cu instead of ♀ for copper. In the year before Berzelius was born a countryman of his died who was to be one of the founders of modern biology—namely, Carl Linnaeus (1707–1778). An exceedingly methodical, industrious, and economical worker, Linnaeus infused these qualities into everything he wrote. Thus his works on the classification of plants (and other natural objects), though encyclopaedic in scope, are distinguished by an economy of style that reflected the man's whole character and frugal way of life rather than his intellect alone. In replacing the old descriptive phrases for each kind of plant by two words, the generic and specific names, he at once introduced a revolutionary simplification into the art of classifying organisms and gave expression to his enthusiasm for orderly brevity in recording his observations. Impelled by this need for economy of writing he used the old alchemical and astrological symbols to denote in his *Species Plantarum* the various types of vegetation, reserving three of them to denote sex. Besides putting ♂ and ♀ for male and female flowers he signified hermaphroditic flowers by ☿, the old symbol for mercury. Following his example biologists the world over have ever since used these symbols in the manner that he originated.

[1] Stearn, W. T., *New Scientist*, August 17, 1961, p. 412.

INTRAMUSCULAR INJECTIONS

For injections of more than a few ml. of most drugs the intramuscular route is preferable to the subcutaneous. Intramuscular injections are less painful, more rapidly absorbed, and less liable to leave nodules or "sterile abscesses." Adrenaline is an exception, for by lowering local oxygen tension it carries the risk of gas-gangrene infection, particularly if given into the buttock.[1] Small intramuscular injections can be easily accommodated in the deltoid muscle, but unless the shirt sleeve is rolled up high the injection may be made so low as to injure the radial nerve. Larger injections should be given into the thigh or buttock. There is plenty of room in the antero-lateral compartment of the mid-thigh, but haematomas are apt to form in the vastus externus muscle.

Nowadays nurses give most intramuscular injections. In the buttock they are taught to use either its upper and outer quadrant or the upper and outer triangle, the latter being the area above a line from the posterior end of the iliac crest to the great trochanter. These are large areas, and if the injection is near the centre of the buttock the sciatic nerve may be damaged.[2] Some instructions therefore advise the nurse to inject "as near the iliac crest as possible." S. Zelman[3] asked 101 nurses about their techniques for intramuscular injection and found that nearly all used the upper and outer quadrant, but eight of them had encountered pain or numbness in the foot after injection. A. von Hockstetter[4] made a detailed study of the published records of the damaging effects of injections into the buttock. In 1954 he had advocated the anterior (ventral) part of the upper and outer quadrant as the best place.[5] The use of this site is not new, however, for it had been employed in venereal-disease clinics for many years. It has many advantages. The gluteus medius and minimus muscles in the anterior gluteal site provide a greater thickness of muscle than does the more posterior gluteus maximus. It contains no important nerves or blood vessels and a too deep injection into it can reach only bone. Also there is less subcutaneous fat than

[1] Tonge, J. I., *Med. J. Aust.*, 1957, **2**, 936. See also *Brit. med. J.*, 1961, **1**, 730.
[2] Capener, N., *Brit. med. J.*, 1956, **1**, 1541.
[3] Zelman, S., *Amer. J. med. Sci.*, 1961, **251**, 563.
[4] von Hockstetter, A., *Schweiz. med. Wschr.*, 1955, **85**, 1138.
[5] —— ibid., 1954, **84**, 1226.
[6] von Richenberg, H. K., and Schmidt, R., *Med. J. Aust.*, 1958, **88**, 37.

posteriorly and so less risk of the injection becoming subcutaneous. It is an area less likely to faecal contamination. The site of a ventral gluteal injection is easily found by palpation. The old method was to choose a point far forward on a horizontal line mid-way between the anterior superior spine and the top of the great trochanter. H. K. von Richenberg and R. Schmidt[6] recommend that for a right-handed operator injecting the right buttock the left index finger be placed vertically with its tip on the anterior superior iliac spine and the middle finger abducted (as in Sir Winston Churchill's V for victory sign) with its tip just below the iliac crest. The injection site is then within the triangle formed by the fingers and the iliac crest.

The position of the patient would not seem to be very important. An injection into relaxed muscles is less painful than into contracted ones and is less likely to be forced back into the subcutaneous tissues. So lying is better than standing and the prone position better than the supine, since the patient cannot then watch the injection. If the patient stands he should bear his weight on the opposite leg. To use a short fine needle as a gesture of kindness is mistaken, for it will result in a painful subcutaneous injection. A sharp 2-inch (5 cm.) needle of medium bore (20 S.W.G.) is best.

Refinements in intramuscular technique are to draw the skin and subcutaneous tissues aside before inserting the needle so that when they slide back the needle track is broken, to aspirate for 5 or so seconds after insertion to make sure that a blood vessel is not entered; to inject a bubble of air or a little physiological saline to clear the needle, and to leave it in place for a few seconds before withdrawal and then to press firmly on the site.

CHEST RADIOGRAPHY OF IMMIGRANTS

The report[1] of an inquest this week on an immigrant who died of tuberculosis a month after entering the country draws attention again to a matter that has caused much concern to the medical profession. The immigrant was a 30-year-old West Indian woman. A chest physician said in evidence that the woman was admitted to hospital with signs of gross disease eleven days after her arrival here. She was so weak she could hardly walk and she must have had tuberculosis at least six months before leaving the West Indies. The coroner, returning a verdict of death from natural causes, advocated a rigid examination before immigrants receive a passport or arrived in Britain.

The Annual Representative Meeting of the B.M.A. passed the following resolution[2] in 1960: "*Resolved:* That this Representative Body asks Council to re-examine the problem of making medical evidence of clean health a prerequisite for the admission of immigrants to the U.K. on a standard form to be approved by the World Health Organization." In subsequent discussions with Government officials it became clear that the Government is reluctant to depart from its traditional policy of not imposing a medical check on immigrants from Commonwealth countries. Apart from the political objections to having compulsory examinations, medical objections are advanced. One is that the examinations would have to be done in the immigrant's own country and the reliability of them would vary greatly from one country to another. Again it is said that immigrants may be more likely to break down with tuberculosis in Great Britain than are the inhabitants of these islands, but they do not necessarily bring the disease into the country.

Nevertheless the problem should not be shelved, for probably few medical men would dissent from the resolution passed this year by the Representative Body when it returned to the question: "*Resolved:* That this Representative Body views with concern the continued admission of immigrants to the U.K. without medical check and considers that all immigrants should have a chest *x*-ray in order that those found to have active lesions may be advised on how best to obtain proper treatment."

[1] *Daily Telegraph* September 12.
[2] *Brit. med. J. Suppl.*, 1961, **1**, 162.

MEDICO-LEGAL SOCIETY'S DIAMOND JUBILEE

This year the Medico-Legal Society—whose aim is "the furtherance of medico-legal knowledge in all its aspects"—celebrates its diamond jubilee. It might have been celebrating it 14 years ago had not the first attempt at starting such a society foundered in 1887. A second attempt met with success in 1901, when Dr. R. Henslowe Wellington, who had practised medicine and read law, decided that the two disciplines might usefully be combined in a wider sphere. Almost immediately the newly formed Medico-Legal Society attracted 65 members, consisting of medical men, members of the legal profession, and what the founder described, in inverted commas, as "intelligent laymen".

Since then the Medico-Legal Society has steadily prospered and has numbered among its presidents such distinguished members of the two professions as Lord Riddell, Sir Bernard Spilsbury, Mr. Justice Humphreys, Sir Roland Burrows, and Sir Norwood East. Dr. Keith Simpson has recently been elected president and is the first forensic pathologist since Spilsbury to take the presidential chair.

The Society's publication has prospered, too, from its beginnings in 1902 as *Transactions of the Medico-Legal Society*, through its change to the *Medico-Legal and Criminological Review* in 1933, to its second metamorphosis in 1947 as the *Medico-Legal Journal*.

Unlike the younger, more specialized societies dealing with forensic medicine, the Medico-Legal Society's aim has always been to act as a forum for broad general discussion of current problems, and to provide what has been described as "the kind of medicine lawyers can understand and the kind of law doctors can understand." In the last 60 years the Society, with its journal, has played an invaluable part in helping those who are professionally interested to follow developments in the medico-legal world brought about by scientific and social change, and its steady growth reflects an increasing recognition on the part of public and police of the importance of this field of study.

UNIVERSITY OF HONG KONG'S GOLDEN JUBILEE

BY

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The University of Hong Kong was founded in the year 1911, owing largely to the foresight of Sir Frederick Lugard, later Lord Lugard, at that time Governor of the Colony of Hong Kong. As in many other places, university foundation had been preceded by the establishment of a medical school, the Hong Kong College of Medicine for Chinese started by Patrick Manson and James Cantlie in 1887. One of the earliest photographic records is that of James Cantlie teaching osteology in 1889 to a group of students dressed in traditional Chinese costume. Among this group of students is Sun Yat-Sen, later to become the founder and first president of the Chinese Republic in 1911. At this time most of the clinical teaching was carried out in the Alice Ho Miu Ling Hospital run by the London Missionary Society.

The Hong Kong College of Medicine continued formal instruction until 1912, the year in which the University opened its doors. All students were then transferred to the Faculty of Medicine, and those who had just graduated were given an opportunity to take degrees of M.B., B.S. after two years' further study. Only one student succeeded in the first examination, Dr. G. H. Thomas, who became the first graduate in the new University in 1914. He subsequently added to his list of "firsts" by becoming the first M.D. in 1920, the first local graduate to become the deputy head and later acting head of the Government Department of Medical Services, and later still the first graduate of the University to be made a Fellow by election of the Royal College of Surgeons of England. A distinguished career has been capped by his admission in this jubilee year to the degree of Doctor of Laws *honoris causa*.

[*Department of Surgery, Hong Kong University*

James Cantlie teaching osteology in 1889.

The Pre-war Decades

In the period between its foundation and the second world war the University as a whole and the Medical Faculty in particular went through a period of slow but progressive development. In the early 1920s the Rockefeller Foundation provided funds to endow the chairs in clinical subjects. A few additions to buildings were made, but student numbers remained quite small. In 1937 the old Government Civil Hospital in a densely populated area of the town was closed as a general hospital, and teaching transferred to the newly built Queen Mary Hospital on the western slopes of the hill four miles from the centre of the town and two miles beyond the University. This hospital is still in use but is in need of considerable expansion and modernization, which is only just commencing.

Occupied by the Japanese

Hong Kong was occupied by the Japanese for 3½ years. The University was closed, buildings looted, damaged, or destroyed, and students dispersed, and at the end of the war there was doubt in some quarters as to whether it should reopen at all. Eventually wisdom prevailed, and it was decided not merely to reopen but to expand, and capital was made available from H.M. Treasury, the Colonial Development and Welfare Fund, and the Hong Kong Government for re-establishment and some new buildings. New members of staff were recruited commencing in 1948.

[*Hong Kong Government Information Services*

The Queen Mary Hospital, Hong Kong.

The first students to graduate after the war were those whose studies had been disrupted and who had continued their education in China, but by 1952 the first group of students graduated who had received all their clinical training in the University.

The Chinese revolution in 1948 and the establishment of the People's Republic was not without its effect on the University and the Colony as a whole. Refugees started to pour into Hong Kong, among them a few who could be admitted as students on transfer from certain reputable universities on the mainland. Many of these universities had been supported by foreign funds. The most prominent medical school of all, the Peking Union Medical College, had been supported by the China Medical Board of New York, Inc., an offshoot of the Rockefeller Foundation. Financial support formerly available for Peking now became available for the other universities in the Far East, and the Medical Faculty of the University of Hong Kong has received many grants for capital equipment and study and travel fellowships from the China Medical Board. So generous has this support been that it is difficult even to imagine what would have been the state of the Faculty had it been dependent on the University's own resources.

After the War

Development in the post-war years has proceeded at a rapid rate. At the present time 68 students are admitted annually, although there have been years when this number has been exceeded. In 1963 it is hoped that a new preclinical building will be opened close to the Queen Mary Hospital, and when this takes place the annual intake will be increased to 100. A new dental school is planned with an annual intake of 25, but this will depend upon the creation of a dental hospital by the medical department of the Hong Kong Government. The new preclinical centre, which will be built partially from Colonial Development and Welfare Funds and partially from a local government subvention, will house the departments of anatomy (including histology), physiology (including pharmacology), biochemistry, social medicine, the animal house, various interdepartmental laboratories and student cloakrooms, the dean's offices, and a separate wing with three large lecture theatres. The site will allow for development in the future and may permit a faculty library, student canteen, and accommodation for clinical clerks in immediate proximity to the hospital.

In 1958 a new building was opened for the department of pathology, also very close to the Queen Mary Hospital. This, which provides for morbid anatomy, parasitology, bacteriology, and clinical pathology, was largely equipped by grants from the China Medical Board and has recently been enlarged by the development of a virus unit equipped and staffed by the Hong Kong Government.

The Tsan Yuk Hospital, a modern maternity hospital with 230 beds, was opened in 1954. Here, during a five-week period of residence, the student will usually conduct, under supervision, at least 50 deliveries, and recently there have been several Chinese students studying in English universities who have elected to return to Hong Kong to do their obstetrical clerkships.

Jockey Club Gift

A new nine-story polyclinic was opened in 1960, built by Hong Kong Government from a donation by the Royal Hong Kong Jockey Club. Within this building, the University clinical departments occupy three floors, and conduct consultation clinics in general medicine, surgery, and in all the various specialties. These three floors have been designed not only to be able to see the very large number of patients who attend but to make full use of them for teaching purposes. These three floors are without doubt the most valuable addition to teaching facilities that the University has ever had.

A further extension to the Queen Mary Hospital is still in the planning stage, but may be available by 1964. It will provide laboratories and teaching facilities at the main hospital for the five principal clinical teaching departments: medicine, paediatrics, surgery, orthopaedics, and gynaecology. The occupation of this building and additional extensions planned in the hospital itself will make available a further 180 beds, most of which will be used for teaching.

[*Hong Kong Government Information Services*

Polyclinic donated by Royal Hong Kong Jockey Club.

During the present jubilee year a new Library and Students' Union will be completed and opened, and it is appropriate that the council should have commissioned a bust of Lord Lugard, by Mr. C. d'O. Pilkington Jackson, to stand in the entrance hall of the Library. The bust, which depicts Lugard in official Colonial uniform but wearing his chancellor's gown, was exhibited at the Portrait Sculptors Society Exhibition in London last year and received very favourable comment.

Active Research Programme

The record of medical graduates has been outstandingly good. Three have held the position of Director of Medical and Health Services either in the substantive appointment or have acted for long periods. Others have become prominent in political fields, being members of urban, legislative, or executive councils. The specialist appointments in Government Service in medicine, surgery, obstetrics and gynaecology, orthopaedics, paediatrics, and radiology are all held by Hong Kong University graduates. Out of 50 whole-time teaching appointments in the Faculty, 20, including three of the eight chairs, are held by the University's own graduates and only eight by expatriates.

All departments of the Faculty are pursuing active experimental or clinical research programmes, and in clinical fields especial interest is paid to diseases which are particularly common and in which there are therefore special opportunities. Thus much work has been carried out and reported on cirrhosis, clonorchiasis, carcinoma of the liver, and portal hypertension, splenomegaly, hypersplenism and disorders of coagulability of the blood, chorionepithelioma, tuberculosis of bones and joints and especially of the spine, and the treatment of drug addiction, as well as much other work of pure scientific interest.

In all, the University of Hong Kong and its Medical Faculty is intensely active, is expanding rapidly, and is looking forward to its second fifty years as an era of even greater productivity.

SURGEONS IN DUBLIN

The Nineteenth Congress of the International Society of Surgery was held in Dublin last week under the presidency of Professor E. DAHL-IVERSEN (Copenhagen). Mr. T. J. C. O'CONNELL (Dublin) was the secretary of the Congress and chairman of its Irish Committee. Later in the week the International Society of Surgery was joined by the International Cardiovascular Society, whose fifth Congress this was. About 1,500 surgeons attended the meetings.

Dr. SEAN F. LEMASS, Head of the Irish Government, gave an address of welcome at the opening ceremony on September 3, and on the following days there were sessions on the surgery of the endocrine glands, on gastro-enterology, on cardiovascular diseases, on the surgical management of occlusive disease of the visceral arteries, and on deep hypothermia in cardiac surgery.

Three memorial lectures were given during the course of the two congresses—the first Grey Turner Memorial Lecture by Professor LAMBERT ROGERS (Cardiff) (reported below); the René Leriche Memorial Lecture, given as the presidential address at the Fifth Congress of the International Cardiovascular Society by Professor CHARLES G. ROB (Rochester, N.Y., U.S.A.); and the Rudolph Matas Memorial Lecture by Dr. A. OCHSNER (New Orleans).

THE FIRST GREY TURNER MEMORIAL LECTURE

[BY A SPECIAL CORRESPONDENT]

Ten years ago George Grey Turner died on the eve of his 74th birthday, accepted the world over as the doyen of British surgery. Northumbrian born and bred, a graduate of Durham, he had won for himself a world-wide reputation as a teacher of surgery and a fearless operator of marked originality. Long before his translation to London his clinic in Newcastle had been as a Mecca to surgeons, British and foreign alike. His life of active teaching thus knew two phases: the first as a provincial surgeon in a small university town set in the wilds of the northern hills and valleys, the second among the millions of a crowded metropolis, with its Royal College of Surgeons, the palladium of Hunter's great collection of pathological specimens—the greatest the world has yet known—which was to become his special care. To all of these he had given his best—and all of it was good.

One of the highlights of the joint meeting of the International Society of Surgeons and the International Society of Cardiovascular Surgery at University College, Dublin, last week was the delivery of the first Grey Turner Memorial Lecture, founded by his widow, who with other members of the family were happily present for its delivery to an audience which crowded the Coffey Hall to its doors. The choice of the first lecturer had been a particularly happy one. Professor LAMBERT ROGERS had been Grey Turner's first reader in surgery on his appointment as professor of surgery in London University, remaining with him as chief assistant throughout his complete tenure of office. Together they had seen the birth of this new department of surgery and had inaugurated the postgraduate courses to be given there in an old municipal hospital building; together they had purchased much of its necessary new equipment and interviewed those seeking appointment as future members of its staff. During the years that followed there grew between these two devotees of surgery a degree of mutual intimacy and regard comparable to that which had enriched the co-operation of the younger "G.G." and his first chief, Rutherford Morison. On Turner's death Rogers, with another close friend, Sir Gordon Gordon-Taylor, had paid eloquent obituary tribute, jointly and separately, to their departed colleague and friend.

The Historical Method

In this memorial, Turner fashion, Professor Rogers illuminated his text with many slides, mostly photographs of the great contemporaries with whom Turner had forgathered in both hemispheres—Paget, Osler, Morison, Matas, and others whom most of his audience in Dublin were too young to have seen in the flesh. With Osler, Turner believed that by the historical (biographical) method alone can many problems in medicine be approached with profit. Thus Professor Rogers drew for us a compelling picture of "G. G.'s" personality, of his unfailing kindness to all, however humble, who came to him seeking aid in their affliction; of his never-failing memory of his patients, their names and those of their families; of his professional honesty and integrity, comparable to that of a Billroth or a Colles. "I doubt," said Gordon-Taylor, whom he quotes, "if any surgeon of our land has ever boasted an experience comparable with his." Gordon-Taylor had been his patient as well as his friend, and his description is too accurate to miss:

> "A man of simple tastes who lived, dressed, and ate simply; his favourite drink was strong tea. Was any surgeon ever so worshipped by his patients? If he ventured to walk the street with that characteristic gait of his, his bowler hat seemingly too big and perched on the back of his head, his progress would be constantly stopped by those who were his devoted patients. He remembered them all . . . the ready sympathy was all there, so genuine. How it helped. He had the simplicity of true greatness, and, like all great men, was absolutely free from self-consciousness."

In the clinic he was not alone a fine surgeon, but a good doctor, never at a loss to suggest something for the good or comfort of his patient, and admonishing his housemen: "Last, but not least in each perplexing case, learn the sweet magic of a cheerful face," adding for good measure that their case notes "should be written like a telegram, everything essential, nothing unnecessary."

Master Word in Medicine

For "G. G.," as for Osler, the master word in medicine was "work." To a Boston audience he quoted with full approval Paget's statement: "The burden of my address is work, lifelong work. And so it is and so it must be: there is no success without it." His own life, right to the end, fully exemplified Kipling's "filling of the unforgiving minute with sixty seconds' worth of distance run."

Grey Turner was a general surgeon, but of a class that our students will never see again. No "specialist," yet he excelled in those very procedures which to-day are the regions of the State-decreed specialisms: his chief interests lay in the surgery of the abdomen, the oesophagus, the ureters, and against the invasion of cancer he waged incessant and successful war. His was a life of hard work devoted to the advance of surgical knowledge on behalf of humanity. As with Osler, loving his profession, he was content to live in it and for it. A great traveller in search of knowledge, he was revered and loved by those who had the good fortune to know and to work with him, and those who had not should learn something of his character and of his work. These should endure in our memories for as long as men value honour, high standards of work, character, and sense of duty.

ROUTINE IMMUNIZATION AGAINST INFECTIOUS DISEASES

The following memorandum, which the Ministry of Health is sending to all general practitioners and medical officers of health, has been prepared on the basis of the advice given to the Minister by the Standing Medical Advisory Committee.

1. It is now possible to provide protection against several infectious diseases in early life by active immunization and there has recently been considerable debate as to the most satisfactory timing of the different immunizing procedures. In this context three considerations seem to be of particular importance:

(i) The greatest possible measure of immunity should be provided against each particular disease.

(ii) There should be the least risk of causing harmful reactions or complications, and, in particular, of inducing provocation poliomyelitis.

(iii) The number of injections given to the child and the number of visits necessary should be as low as possible.

2. No single schedule can fully meet all these considerations, and the two alternative schedules printed below are different attempts to reach a compromise. Modification of these schedules may be necessary later in the light of rapidly advancing knowledge in this field. Attention is drawn in the following paragraphs and in the notes to each schedule to factors which will be of importance in deciding which schedule is most suitable. In some cases it may be desirable to modify one of the schedules to meet special circumstances.

3. In general, the ability to form antibodies in response to an antigenic stimulus is immature at birth and may not be fully developed until about 6 to 9 months of age. Although a useful response is to be expected before that age, it may not be maximal. Another factor which may affect adversely the ability of the infant to respond to active immunization is a high level of maternally transmitted antibody. For these reasons vaccination against poliomyelitis, for example, is deferred until the infant is at least 6 months old.

4. The use of combined antigens requires a careful balance between them in order to prevent the response to one antigen overwhelming that to other antigens. The manufacturers of combined antigens recognize the importance of this.

5. It has been shown that the use of certain combined antigens—for example, a combination of pertussis vaccine and diphtheria toxoid—carries a slight risk of provocation poliomyelitis — that is, poliomyelitis occurring within a few days of injection with paralysis particularly affecting the site of inoculation. However, the risk of such cases occurring is much less than in past years, and there is reason to believe that they will not become more frequent if the prevalence of poliomyelitis in the population remains low. The objection on this ground to the use of combined antigens is therefore considerably reduced.

6. It is a reasonable assumption that poliomyelitis vaccination will protect against provocation paralysis although this has not been demonstrated in man.

7. The number of deaths from whooping-cough has been falling very considerably for several years. Deaths after the first year of life are rare. The majority of deaths occur in the first six months of life, so that even very early immunization is unlikely greatly to reduce these deaths. The time of maximum incidence of the disease, as judged by notification figures, is from 1 to 4 years.

8. In general, there are advantages in immunizing children at a time which would ensure that their resistance to infection will be at its height when the risk of exposure is greatest. It is possible, however, that a mother can be more readily persuaded to accept immunizing procedures if the first approach is made early in the child's life.

9. It is considered desirable to offer immunization against poliomyelitis at about the age of 7 or 8 months with a reinforcing dose after the fourteenth month, against diphtheria between 9 and 12 months with reinforcing doses after the eighteenth month and before school entry, and against smallpox at 4–5 months of age. Immunization against whooping-cough may be started either in the early months of life or, towards the end of the first year, before the time of maximum incidence of the disease. It seems unlikely, in view of the relative mildness of whooping-cough after the first year, that reinforcing doses are indicated against this disease. It will also be desirable to offer immunization against tetanus in the first or second year, with a reinforcing dose before school entry. These points are discussed in more detail in relation to each of the schedules.

SCHEDULE P

Age	Visit	Vaccine	Injection	Interval
1 to 6 months	1	Diphtheria, pertussis, tetanus 1	1	
	2	Diphtheria, pertussis, tetanus 2	2	4–6 weeks
	3	Diphtheria, pertussis, tetanus 3	3	4–6 „
7 to 10 months	4	Poliomyelitis 1	4	4 „
	5	„ 2	5	
15 to 18 months	6	„ 3	6	
18 „ 21 months	7	Diphtheria, pertussis, tetanus 4	7	
Smallpox during the first 2 years but preferably at 4–5 months (see Note *h*)				
School entry ...		Poliomyelitis 4, diphtheria and tetanus		
8 to 12 years ...		Diphtheria and tetanus. Smallpox revaccination		
Over 12 „ ...		B.C.G. (see Note *i*)		

NOTES

(*a*) Pertussis vaccine is given early in the hope of reducing the incidence and severity of whooping-cough in infancy.

(*b*) There is no real need to give diphtheria and tetanus toxoids so early in life, as the incidence and death rates from those diseases below the age of 1 year are almost negligible.

(*c*) The use of a combination of a bacterial vaccine and two toxoids may increase the incidence of "provocation" paralysis.

(*d*) The first injection is given in early life, at which time the mother is more likely to accept advice about immunization matters.

(*e*) A practical argument for this schedule is that it is at present being used (possibly with minor modifications) by a number of local health authorities and general practitioners.

(*f*) The number of visits and injections is greater than in Schedule Q

(*g*) Should it be desired, visit 7 may be avoided by giving poliomyelitis 3 and diphtheria/pertussis/tetanus 4 at different inoculation sites during visit 6.

(*h*) An interval of at least two weeks should normally be allowed to elapse after an injection of diphtheria/pertussis/tetanus or poliomyelitis vaccine before undertaking vaccination against smallpox. When vaccination against smallpox precedes

an injection of one of the other vaccines it is desirable to allow at least three weeks to elapse.

(*i*) B.C.G. vaccine may be given to schoolchildren aged 10 years or more at the discretion of the Medical Officer of Health. (Circular 6/61.)

SCHEDULE Q

Age	Visit	Vaccine	Injection	Interval
6 to 8 months	1	Poliomyelitis 1	1	4 weeks
	2	„ 2	2	
9 to 12 months	3	Diphtheria, pertussis, tetanus 1	3	4–6 weeks
	4	Diphtheria, pertussis, tetanus 2	4	
15 to 18 months	5	Poliomyelitis 3	5	
18 „ 21 „	6	Diphtheria, pertussis, tetanus 3	6	
Smallpox during the first 2 years but preferably at 4–5 months (see Note *f*)				
School entry ...		Poliomyelitis 4, diphtheria, and tetanus		
8 to 12 years ...		Diphtheria and tetanus. Smallpox revaccination		
Over 12 „ ...		B.C.G. (see Note *g*)		

NOTES

(*a*) On this schedule, no antigen is given *by injection* before the age of 6 months, which increases the possibility of a maximal antibody response.

(*b*) Two doses of poliomyelitis vaccine are given before any other injection, and, although it cannot be accepted as proved, this might well reduce the risk of "provocation" paralysis which would otherwise be increased owing to the use of the combination of pertussis vaccine with toxoids.

(*c*) Vaccination against pertussis is delayed until between 9 and 12 months; thus no direct protection is offered against the risk of death among younger infants. On the other hand, the time of vaccination in this schedule is nearer to the time of maximum incidence of the disease, and this may indirectly protect infants by reducing their chances of being infected by older children.

(*d*) The number of visits and injections is smaller than in Schedule P, but it is possible that if immunization is postponed until the baby is six months old it may be less easy to gain the continued co-operation of the parents. Early vaccination against smallpox would, however, help to keep the mother in touch with the doctor.

(*e*) Should it be desired, visit 6 may be avoided by giving poliomyelitis 3 and diphtheria/pertussis/tetanus 3 at different inoculation sites during visit 5.

(*f*) An interval of at least two weeks should normally be allowed to elapse after an injection of diphtheria/pertussis/tetanus or poliomyelitis vaccine before undertaking vaccination against smallpox. When vaccination against smallpox precedes an injection of one of the other vaccines it is desirable to allow at least three weeks to elapse.

(*g*) B.C.G. vaccine may be given to children aged 10 years or more at the discretion of the Medical Officer of Health. (Circular 6/61.)

NOMENCLATURE OF HAEMOGLOBINS

The following recommendations on the nomenclature of haemoglobins have been sent to us by Professor V. M. Ingram, of the Department of Biology of the Massachusetts Institute of Technology, and Dr. P. S. Gerald, of the Children's Hospital Medical Center and Harvard Medical School, Boston. The proposals originated during a "Haemoglobin Structure Workshop" held in Boston in December, 1960. The recommendations are also appearing in the August issue of the "Journal of Biological Chemistry."

Chain Nomenclature

There is now general agreement on the naming of the peptide chains of the major components of normal human adult and foetal haemoglobins as the α, β, and γ chains—e.g., adult haemoglobin is written as $\alpha_2^A\beta_2^A$ and foetal haemoglobin as $\alpha_2^A\gamma_2^F$. The superscripts A and F refer to the fact that the particular chain is the one found in the human adult and foetal haemoglobins. It is recommended that this practice be continued and that the symbols α, β, and γ, without superscripts, be reserved for those occasions when reference is being made to, for example, chains in general.

Information concerning the structure of the chains of haemoglobin A_2 is now sufficient to indicate that one of the chains is identical with the α^A chain, while the second differs in a number of residues from the three foregoing chains. In addition there is evidence (e.g., Cepellini[1]) to indicate that the genetic control of this unique chain is independent of the genes for the α, β, and γ chains. It is therefore recommended that this chain be designated as δ^{A_2}; Hb A_2 is then written as $\alpha_2^A\delta_2^{A_2}$. Again, one could refer simply to δ chains in the general case.

The simplest method of naming the tryptic peptides of a chain is to number them in the order in which they occur in the chain, beginning with the N-terminus. The symbol for the chain is included as a part of the designation. The letters Tp are included to identify that these are the peptides obtainable by tryptic digestion. For example, the third tryptic peptide of the α chain would be αTpIII in this system. Where a lysyl bond is not attacked under the conditions used, the symbol for the resultant "dipeptide" or "double peptide" would contain the numbers appropriate to both tryptic peptides—e.g., αTpI,II. From the published structure of the α and β chains[2–4] and from the amino-acid composition, it is evident that the α chain will contain the tryptic peptides αTpI to αTpXIV and the β chain the tryptic peptides βTpI to βTpXV. It so happens that the tryptic "peptides" αTpVIII and βTpVIII are lysine. In addition, the present methods of tryptic cleavage do not break the bond separating the expected tryptic peptides αTpXII and αTpXIII, nor the bond between the expected peptides βTpX and βTpXI. In view of the possibility that these bonds might be split in some experiments at a later date, it is felt that the numbering system should correspond with the theoretical number of tryptic peptides. When the complete sequence of the chains is determined beyond question and is published, then a more specific designation involving residue numbers should be adopted. Thus, βTpI can be designated as βTp1–8.

Nomenclature of Abnormal Haemoglobins

An ideal nomenclature system for the abnormal haemoglobins would provide for adequate designation of the chemical structure at each stage of the investigation. The following system is an attempt to meet this requirement.

When only the chain in which the abnormality resides is known, then the haemoglobin may be written as $\alpha_2^A\beta_2^S$, or $\alpha_2^A\beta_2^{D\text{Punjab}}$. When the abnormality has been located in a particular tryptic peptide, as by fingerprinting, then the designation should be, for example, $\alpha_2^A\beta_2^{\text{TpI}}$. When the amino-acid composition of the tryptic peptide indicates a particular amino-acid substitution, then this will be indicated as $\alpha_2^A\beta_2^{\text{TpI(Glu}\rightarrow\text{Val)}}$ for Hb S. Finally, when the amino-acid interchange has been located at a particular residue position in the chain, the fully descriptive formula, as in the case of Hb S, would be in the form : $\alpha_2^A\beta_2^{6\text{Val}}$.

Presumably, for use in formulae describing experiments such as reassociation, it will be necessary to define in a given paper a one-letter designation for a particular haemoglobin. For example, the formula $\alpha_2^I\beta_2^S$ could be used, provided that wherever possible the individual haemoglobins have been defined, as, for example, Hb I as $\alpha_2^{16\text{Asp}}\beta_2^A$ and Hb S as $\alpha_2^A\beta_2^{6\text{Val}}$. It is strongly urged that no further letters be assigned to abnormal haemoglobins. Newly discovered haemoglobins, prior to their chemical identification, should be known by the letter designation of the previously described haemoglobin whose electrophoretic mobility they most nearly resemble. To the letter should be attached a subscript indicating the geographic origin of the new haemoglobin.

(*Continued at foot of page 765*)

To-day's Drugs

With the help of expert contributors we publish below notes on a selection of drugs in common use.

Meprobamate

"Equanil" (Wyeth).
"Mepavlon" (Imperial Chemical (Pharmaceuticals)).
"Miltown" (Wallace).

Chemistry.—This is 2-methyl-2-n-propyl-1:3-propanediol dicarbamate.

Pharmacology.—Although chemically related to the muscle-relaxant drug mephenesin, mebrobamate has little effect as an internuncial depressant. It produces sedation, with general slowing of the electroencephalograph, and has an effect on the higher parts of the central nervous system at least as much as on the lower. Most of the experimental work has compared meprobamate with chlorpromazine and other newer tranquillizers. Comparisons with barbiturates have not been properly carried out, but it is known that meprobamate and barbiturates are synergistic. The drug is comparatively non-toxic.

Therapy.—Meprobamate is said to be a mild tranquillizer, a class of drug that is considered in itself to have less hypnotic effect than, say, barbiturates, so it is perhaps hardly surprising that the drug has little therapeutic effect. In some tense patients it is undoubtedly effective as a mild sedative, but, in spite of being chemically related to the muscle-relaxant mephenesin, it is of no special value in treating those patients with prominent muscular tension and secondary "rheumaticky" pains—e.g., at the back of the neck. Clinical studies make it doubtful if it is better than phenobarbitone for psychiatric disturbances; it is of less value for the more seriously disturbed patients, including psychotics. In neurological diseases entailing spasticity of muscles, meprobamate sometimes decreases the muscle spasm, and even patients with Parkinsonism may be benefited.

Meprobamate has perhaps a small place as one of the group of drugs producing mild sedation, ringing the changes on which will enable some chronically tense patients to be kept going. It has no specific advantages over any other such drug, nor is there any unique indication for its use. The drug acts synergistically with other sedatives, including barbiturates, but combined treatment gives a false impression of getting the same sedation with less "drugging," since meprobamate is not freer than barbiturates from undesirable depressant effects.

Toxic Effects.—A wide variety of toxic effects have been reported, but most of them are rare. Skin rashes of all sorts are the commonest, and general hypersensitivity reactions next. Habituation, and even addiction, can occur, but very rarely. After heavy and prolonged administration, abrupt withdrawal will produce a syndrome of tremulousness, gastrointestinal disturbances, and sometimes convulsions. Suicide can be successfully committed with meprobamate.

N.H.S. Basic Price.—400-mg. tabs., 100 for 15s. 5½d.

(*Continued from page 764*)

Proposals similar to the above originated during the Haemoglobin Structure Workshop held in Boston, December 14–16, 1960. These proposals have been modified at the suggestion of other workers in the protein-structure field. In their present form they represent a compromise between the views of these two groups.

REFERENCES

1 Cepellini, R., Contribution to Ciba Symposium on Biochemical Genetics, 1959.
2 Braunitzer, G., Rudloff, V., Hilske, K., Liebold, B., and Mueller, R., *Hoppe-Seylers Z. physiol. Chem.*, 1960, **320**, 283.
3 —— ibid., 1960, **322**, 96.
4 Hill, R., and Konigsberg, W., *J. biol. Chem.*, 1961, **236**, PC7.

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Seasonal Incidence in Clinical Onset of Hodgkin's Disease

SIR,—We have been much interested in the report from the Royal Marsden Hospital by Dr. Marion D. Cridland (September 2, p. 621) suggesting a seasonal incidence in the clinical onset of cases of localized Hodgkin's disease, many of which appear to arise in the month of December. As Dr. Cridland indicates that comparable studies might be made elsewhere and as we are at present reviewing a series of 440 histologically proven cases seen at the department of radiotherapy at Edinburgh Royal Infirmary since 1936, we have abstracted the relevant figures from this group.

We have followed exactly the criteria adopted by Dr. Cridland for the selection and exclusion of cases, so that the results should be as closely comparable as possible. In the Royal Marsden series of 269 cases 106 were accepted as true localized cases, whereas in the Edinburgh series a much smaller proportion, 104 out of 400 cases, could be similarly classified. In these the ratio of males to females was 2:1, the same as in the London group. The Table below has been drawn up in the same manner as Dr. Cridland's results were presented to show the seasonal onset of cases in the Edinburgh and London series and in the combined series of 210 cases.

Month of Onset	Edinburgh (104 Cases)		London (106 Cases)		Combined Series (210 Cases)	
	No.	%	No.	%	No.	%
January	19	18·2	14	13·2	33	15·7
February	11	10·6	6	5·7	17	8·1
March	13	12·5	4	3·8	17	8·1
April	4	3·8	9	8·5	13	6·2
May	1	0·9	7	6·6	8	3·8
June	9	8·6	7	6·6	16	7·6
July	13	12·5	4	3·8	17	8·1
August	6	5·8	6	5·7	12	5·7
September	2	1·9	12	11·2	14	6·6
October	15	14·4	5	4·7	20	9·5
November	5	4·8	9	8·5	14	6·6
December	6	5·8	23	21·7	29	13·8

It will be seen that, while the Edinburgh figures show a more random distribution of seasonal incidence, 41.3% of the cases occurred between January and March, and in the combined series December and January are undoubtedly the months of maximum incidence.

Having made this study to compare with Dr. Cridland's findings we feel hesitant to draw conclusions regarding a possible causal infective agent in the disease. It must be realized that the results are entirely dependent on the ability of patients to recall the month in which they first noticed enlarged lymph nodes. Unless the nodes had enlarged rapidly there is no way of being certain that the onset of the disease occurred in this month, and furthermore it is a not uncommon experience to discover quite large superficial nodes of which the patient is unaware.

As the cause of Hodgkin's disease and other reticuloses remains unknown it would seem that the need continues for all studies that may throw further light on the natural history of these disorders.—We are, etc.,

JAMES INNES.
JOSEPH NEWALL.

Royal Infirmary, Edinburgh.

Obstruction of Central Retinal Artery Associated with Chorea

SIR,—The interesting case described by Dr. G. W. Hearn and Mr. M. J. Roper-Hall (September 9, p. 684) reminded me that 35 years ago, while assistant to the late Professor J. Shaw Dunn, I commented on the condition of the brain in two fatal cases of chorea. The opportunities for such studies are rare and I feel justified in recalling them.

In my first case there was diffuse hyperaemia of the cerebral tissue and pia-arachnoid but no focal lesions were found; in the second there was no hyperaemia, but innumerable softenings in the white matter were present and in each of these examined there was a small arteriole "plugged with homogenous material similar to that of the cardiac vegetations."[1] Similar focal lesions were found in the kidneys; they were so numerous in both organs that we concluded they had been formed *in situ* and were not due to emboli. My tentative suggestion at that time was that these pathological changes represented different stages in the vascular lesions associated with chorea; first there may be diffuse hyperaemia, and if this persists long enough focal thromboses occur. Such a hypothesis reconciles the conflicting reports on the cerebral pathology of chorea, but that, of course, does not prove it is correct.—I am, etc.,

Edgbaston, Birmingham. A. P. THOMSON.

REFERENCE

[1] Thomson, A. P., *Bgham med. Rev.*, 1926, **1**, 267.

Aorto-enteric Fistula

SIR,—Following Mr. H. S. Shucksmith and Mr. G. Wilson's interesting medical memorandum (August 26, p. 567) I think it would be worth while reminding your readers that aorto-enteric fistula can occur without surgical aid. We had such a case recently also proved at post mortem.—I am, etc.,

Exeter. K. P. S. CALDWELL.

Spontaneous Delivery of Central Placenta Praevia

SIR,—I have just read with interest the case of spontaneous delivery of central placenta praevia reported by Dr. John Weeks (June 3, p. 1589). I had a similar case here some years ago. I was called to examine a woman just admitted in labour and found the placenta free in the vagina ahead of the baby. I removed the placenta, and with one more contraction the mother expelled a stillborn foetus. Nothing had been said about antepartum haemorrhage until she was asked, and I was amazed at her relatively good condition. She was anaemic but not exsanguinated, and responded well to haematinics. We find it difficult to get blood donors here for any but the direst emergencies.

I wonder how rare it is to have *two* prolapsed arms in a shoulder presentation. We have just seen our first case in 17,000 deliveries, and this was in a primipara. She had been brought seven miles in a bullock cart with both arms pulled out up to the shoulders. One of my colleagues did an amputation of both arms through the shoulder-joints, and delivered the patient by internal podalic version and breech extraction. She did very well and went home on the fifth day.—I am, etc.,

Godavari Delta Mission Women's Hospital, India. BETTY D. HOLT.

Premalignant Conditions of the Vulva

SIR,—We are most grateful to your several correspondents for their comments on our article on premalignant conditions of the vulva which was published in your issue of July 15, 1961 (p. 127). They illustrate and strengthen our arguments even better than we could have hoped. One expert looks at a vulva, or at a section of vulval skin, or at a reproduction of a photomicrograph, and firmly attaches one diagnostic label; another, equally expert, reaches an entirely different conclusion. This is the very point which was emphasized in our paper. Moreover, such differences of opinion are not purely between dermatologists and gynaecologists; they flourish within each specialty. Some of the labels which were sceptically attached to our illustrations were provided by experienced dermatologists and pathologists from centres other than our own.

We realize that those who have built, or become accustomed to, an edifice dislike to see it shattered. New building can be achieved either by destroying the old and starting afresh or by modifying the old. The latter procedure is reasonable only if the original foundations are sound. Your correspondents have produced no argument or evidence to show that those classifications of vulval conditions often used at present are securely founded or, indeed, are anything more than arbitrary and confusing, of no help to the clinician in determining treatment and assessing the risk of neoplastic change. In this latter respect we would emphasize that we did not say that "leucoplakia" is not premalignant. We reached the conclusion that any chronic epithelial dystrophy which on section shows histological evidence of epithelial unrest carries probably a 10% risk of cancer. In the absence of such histological change, however, the risk is negligible.

In again thanking your correspondents for strengthening our case, we would like to join with them in advocating serious and concerted research into the aetiology of the chronic vulval skin changes in question. Only by finding the causes does there seem any real hope of providing the sufferers with rational and effective treatment. If we have succeeded in doing no more than shake the foundations of the present classifications of vulval dystrophies we hope we may have helped towards this end.—We are, etc.,

Liverpool. T. N. A. JEFFCOATE.
A. S. WOODCOCK.

Betamethasone

SIR,—I have read Dr. R. O. Gillhespy's letter on betamethasone (August 12, p. 454) with interest. It appears that his experience with this new corticosteroid in the treatment of rheumatoid arthritis has been unhappy. Dr. Gillhespy's assessment of its potency and value is at variance with the preliminary reports of Drs. J. H. Glyn and D. B. Fox (March 25, p. 876), H. Coke,[1] and others, and also with the results of my own therapeutic trials in a series of some 80 patients. This report is presently being prepared for publication.

I do not question the accuracy of Dr. Gillhespy's clinical observations in his own small series of cases, but I should like to draw attention to four points in his letter bearing upon the pharmacodynamics of betamethasone which seem to me to require correction or clarification.

1. "Betamethasone showed a poor anti-inflammatory corticosteroid effect."—This sweeping statement cannot

be justified on the basis that 12 out of 36 cases of rheumatoid arthritis failed to respond "satisfactorily" to a variable dose of the drug. Our own experimental and clinical pharmacological studies have satisfied us that betamethasone is a powerful anti-inflammatory (anti-rheumatic) steroid preparation.

2. "A degree of unpredictability of effect" was exhibited.—This is true of every corticosteroid preparation which we have studied.

3. The side-effects described must be regarded, at present, as inherent though fortunately inconstant components of anti-rheumatic steroid activity. I know of no evidence to suggest that any one active steroid preparation is more or less likely to produce these side-effects than others.

4. Dexamethasone "differs from betamethasone only by virtue of having the methyl group in the 'beta' position."—This is quite a difference! Indeed, it is probably the most intriguing fact about the new compound.—I am, etc.,

Rheumatic Diseases Unit, Royal Infirmary, Glasgow. J. P. CURRIE.

REFERENCE

[1] Coke, H., *Rheumatism*, 1961, **17**, 70.

SIR,—My experience with betamethasone has led me to believe that it is an effective corticosteroid in the treatment of asthma and rheumatoid arthritis. I agree with Dr. David Williams (August 26, p. 585) that it is all a matter of dose, and in this respect betamethasone suffers a disadvantage in comparison with prednisolone. The aim of steroid treatment in asthma and rheumatoid arthritis is to use the minimum effective dose. It is my practice to prescribe 1 mg. prednisolone tablets for maintenance therapy, since in this way the dose can be reduced by gradual stages. Many patients are doing well on doses of 2 mg. three times a day or even less. Since the "betnelan" tablet of 0.5 mg. is approximately equal in effect to 4 mg. of prednisolone reduction of dose is very much more difficult with betnelan than with prednisolone. Perhaps there should be a smaller betnelan tablet.—I am, etc.,

Whittington Hospital, London N.19. ARNOLD BLOOM.

Nitrous Oxide in Dentistry

SIR,—Is it not possible that the common practice of administering 100% nitrous oxide to induce anaesthesia for dental extractions may be the primary cause of "fainting" in the dental chair? According to Wiggers, as quoted by V. Keating,[1] the onset of anoxia in the human body is at first accompanied by compensatory changes in the cardiovascular system as a result of which the blood-pressure is maintained at a safe level; when the percentage of oxygen in the inspired gases falls below about 7% reduction of cardiac output and vasomotor tone leads to a fall in blood-pressure and ultimately heart failure.

Patients vary a great deal in their response to anoxia, and unless one is gifted with second sight it is difficult to forecast exactly what is going to happen in any particular case. Too sudden deprivation of oxygen, as in the orthodox nitrous-oxide induction, may in some cases disrupt the cardiovascular compensatory mechanism so that it does not function: this is especially likely to happen when the patient is ill-prepared, unsedated, and in a highly emotional state of nervous tension at the prospect of having "gas," but it is also occasionally seen in strongly built, healthy, and apparently well-adjusted adult males.

In the light of present knowledge most anaesthetists would, I think, prefer to reverse the order of the statement attributed to Barcroft by Dr. Arthur Tom (September 2, p. 649) and say that a period of full oxygenation followed by a short period of oxygen lack is likely to be considerably safer than vice versa. So far as my own practice is concerned I abandoned the technique of starting a dental anaesthetic with 100% nitrous oxide some years ago, since when there has been a very marked reduction in the number of patients who require treatment for "fainting" or delayed recovery.—I am, etc.,

Newcastle upon Tyne. PHILIP AYRE.

REFERENCE

[1] Keating, V., *Anaesthetic Accidents. The Complications of General and Regional Anaesthesia*, 2nd edition, 1961, pp. 85–86. Lloyd-Luke, London.

SIR,—Having administered over 90,000 dental anaesthesias I was interested to read the letters by Dr. R. M. M. Fordham (September 2, p. 648) and Dr. Arthur Tom (p. 649). In my experience 14 hours' fasting is far too long before an anaesthetic. There would certainly be some degree of hypoglycaemia present.

I find it best to advise my patients to have a small glucose drink not less than two hours beforehand if the anaesthetic is to be administered at a morning session, where the instructions will have been "No breakfast or milk." Breakfast not later than 9.30 a.m. suffices for an afternoon session, and nothing else. I think most nervousness can be soothed away by the anaesthetist if the sweating and shaking induced by even a mild hypoglycaemia is not present.

I most heartily agree with Dr. Tom and condemn suboxygenation absolutely. I do not allow more than five breaths of 100% nitrous oxide and trilene. The machine is then adjusted to give 15% oxygen (20% for pregnant women and anaemic children), and I find this gives a perfectly smooth anaesthesia. The patient is a good colour throughout and the operating surgeon can have as long as he needs, often 20 minutes.—I am, etc.,

Chigwell, Essex. CONSTANCE P. F. THOMAS.

Abdominal Wound Dehiscence

SIR,—In relation to the recent correspondence on the subject of abdominal wound dehiscence I would like to contribute the following facts.

I operate in three Dublin hospitals—the Rotunda, the Royal City of Dublin, and Monkstown. "Ethicon" catgut is used in all three and I have no reason to criticize this brand of catgut. When the accident of abdominal wound dehiscence occurs it is, in my opinion, more likely to be due to inherent risks such as gross adiposity and wasting diseases than to the rapid absorption of catgut.—I am, etc.,

Dublin. NINIAN MCI. FALKINER.

Medical Aid to Developing Countries

SIR,—I have recently returned from Lagos, Nigeria, after a 27-months' secondment, during which I was to "help organize a comprehensive child health service" for the Federal capital. I have followed with interest the correspondence on secondment, proleptic appointments, and oversea service which arose from Sir

Douglas Robb's presidential address (February 11, p. 375). As I was the author of one of the articles to which he referred, and as I am now more than ever convinced of the importance of assisting developing countries on a basis of "mutual respect and equality" (to quote Sir Douglas), I hope you will allow me to mention some points which have not, I believe, been raised before. An understanding of the problems likely to be encountered even by those most anxious to help may ultimately further the cause of Commonwealth medical co-operation.

In Lagos the Federal Minister of Health has to battle for funds to pay for hospital building, equipment, drugs, salaries, etc. He must organize a medical service commensurate with the potentialities of the community, yet attempt to meet its needs. Integration with the overall economic situation is essential, yet he has to plan for a country whose financial situation is precarious —a situation which faces so many emergent countries. The complexity of this task is becoming daily more difficult owing to the rapid growth of Lagos. The question of priorities is pressing. What comes first; health or schools, drains or communications; slum clearance or agrarian reform? Since there is, as yet, no public opinion sufficiently articulate to bring pressure to bear on other politicians, his fight is a lonely one.

The Minister's permanent medical and lay advisers, grossly overworked, were almost all trained by our Colonial Medical Service. One wonders how well this training fitted them to deal with problems of medical planning and administration compared with which our own National Health Scheme difficulties almost pale into insignificance. A profusely proliferating bureaucratic personnel clogs the administrative machine, and only a drastic pruning would improve matters. Yet the administrators, even if they have the will, do not have the power to remove inefficient lay staff once these have been engaged as permanent civil servants—yet another relic of our own Colonial service.

In a recent issue of the *Journal* (August 26, p. 572) you refer to the vital importance of preventive medicine. Yet in a city like Lagos, where the closest possible co-operation (amounting really to fusion) of the preventive and curative services is essential, mass and individual medicine do not mesh. Thus lives, money, and effort are wasted. Can we blame the Nigerian administrator? Did we teach him in his D.P.H. or D.T.M.H. course how to integrate prevention and cure in a tropical town, without a drainage system, where one half of the 500,000 inhabitants are children?

Since the days of Colonial rule Lagos hospitals have been administered by medical superintendents, some good, some bad, some indifferent. Now the rapidly growing number of specialists demands that their needs be discussed at hospital committee level, and then submitted for approval to some type of hospital board after scrutiny by a mixed lay and medical management committee. However, such a system of administration does not exist. How many Nigerian doctors have been given an opportunity to learn modern techniques of hospital administration? How can the administrator judge the relative urgency of a bewildering (and often irreconcilable) number of demands from the specialists they employ?

Space forbids further elaboration. Many formidable problems have to be faced and solved. The traditional, quasi-military practice of "posting" instead of appointing junior medical staff frustrates both the specialist and the young doctor. Does it make sense to "post" a budding anaesthetist, just returned from postgraduate work abroad, to, say, the paediatric department? Yet the shortage of doctors, and funds to employ them, may well force the administrator to continue this much-hated practice. The distributing machinery for drugs, etc., no doubt adequate 60 or even 30 years ago, is not geared to present-day needs. The reorganization of hospital logistics presents the administrator with a task of extraordinary complexity. Finally, problems of nurse-training loom large. Need the Nigerian nurse know about coeliac diet or the after-care of congenital dislocation of the hip but not about the incidence of paediatric disease in Lagos or the vital role of the public health service? What guidance do we give for the adaptation of the "official" (that is, G.N.C.-based) syllabus to local needs? How many U.K.-trained Nigerian nurses were taught to run a 40-bedded children's ward when the monthly admissions number 300?

Those who are anxious to help new nations in evolving efficient medical services must recognize these and similar problems. Much thought and rethinking will be needed from those who advise on medical organization in developing countries. Only a determined effort to adapt and modernize a traditional pattern will enable these countries to progress at a rate which they have the right to expect. If we don't help, other nations will.—I am, etc.,

Children's Department,
Lewisham Hospital,
London S.E.13.

BRUNO GANS.

Carbon Tetrachloride Poisoning

SIR,—In their article (August 19, p. 493) Drs. J. K. Dawborn, Mary Ralston, and S. Weiden state that damage to the kidney is usually slight when poisoning follows ingestion of carbon tetrachloride. The case they describe would have been classified as subacute by Hardin[1] in his review of 77 cases, and it was realized by Smetana[2] as long ago as 1939 that the kidney lesion in this group was often more important than that of the liver.

So far as ingestion of the poison is concerned this is less commonly met, but rather more rapidly fatal than inhalation of the vapour, hence death may result from liver damage before renal failure has developed. In Hardin's series all 11 cases of ingestion of carbon tetrachloride had clinical symptoms of renal damage, and, though necropsy was performed in only four of them, two of these showed anatomical evidence of renal damage.—I am, etc.,

Aldbourne, Wilts. D. J. STOKER.

REFERENCES

[1] Hardin, B. L., jun., *Industr. Med. Surg.*, 1954, **23**, 93.
[2] Smetana, H., *Arch. intern. Med.*, 1939, **63**, 760.

Patients with Trophoblast Tumours Wanted

SIR,—The observations reported by Dr. Margaret A. Sanders and her colleagues (August 12, p. 454) and not mentioned in their original contribution to *Nature*[1] raise some interesting queries. Does the "relatively structureless mole" contain trophoblast? If so, AzUR would have a differential effect on different parts of the foetus, presuming that trophoblast is of foetal origin. Some chorion carcinomata are believed to originate in hydatidiform moles, so do the writers feel that they are on safe ground by advocating a treatment for chorion carcinoma that produces a mole? Further information would be most helpful.—I am, etc.,

Public Health Offices,
Ilford, Essex.

I. GORDON.

REFERENCE

[1] Sanders, M. A., Wiesner, B. P., and Yudkin, J., *Nature (Lond.)*, 1961, **189**, 1015.

Pigmentation and the Pituitary

SIR,—Your annotation on pigmentation and the pituitary (September 2, p. 634) prompts me to record the impression that leucoderma occurs more frequently

in thyroid disorders than in any other diseases or independently in the population at large. It is not surprising that general pigmentary skin changes should occur where the relationship between the thyroid and the pituitary is disturbed, but there is no obvious explanation why such disturbance should lead to patchy loss of pigment in the skin. Discovery of a link, if any exists, may throw light on the baffling genesis of leucoderma.—I am, etc.,

Selly Oak Hospital, Birmingham 29. A. M. NUSSEY.

Psychopaths Aged over 25

SIR,—Dr. K. C. Bailey has told me, amplifying what he wrote you (August 19, p. 524), that the patient in question, since she left hospital, has yet again attempted her life and been yet again resuscitated and yet again admitted to a psychiatric hospital. Dr. Bailey cites the possibility of the future detention of this patient and her kind through the courts under Section 60 of the Mental Health Act. But since this patient commits no offence other than that of attempted suicide, this recourse will soon be wrested from us by our legislators—and how then shall we cope ?

Some months ago I gave warning in the correspondence column of *The Times* of the danger of this legalization of attempted suicide—so often, in my experience, the irresponsible gesture of the infantile personality. May I, through you, Sir, ask Mr. Kenneth Robinson, M.P., who replied in opposition to me, and his fellow supporters of this Bill in the House of Commons, how society will be expected to manage such cases once our last means to the urgently needed medical grip upon them has been removed ?—I am, etc.,

Exeter, Devon. SEYMOUR SPENCER.

Intravenous Iron

SIR,—I have read with interest the article by Dr. J. Fielding (July 29, p. 279) on intravenous iron-dextrin in iron-deficiency anaemia, and would like to report that in 1956 we undertook a clinical trial at the Holdsworth Memorial Hospital, Mysore, South India, in the treatment of iron-deficiency anaemia using intravenous saccharated oxide of iron. A course consisted of ten injections, starting with 2 ml. diluted with the patient's blood to 10 ml. If there were no reactions the daily injections were begun. Two series of trials were conducted with about 25 men aged between 18 and 25 years in each group. One group was given "iviron" (saccharated iron oxide) and the other "iviron with cobalt" (saccharated iron oxide with a trace of cobalt). The results were very interesting. The group receiving iron with cobalt showed a very rapid rise in haemoglobin level, reaching the 100% mark in under ten days —e.g., six to seven days—whereas the group receiving the iron without the trace of cobalt took anything from 11 to 15 days before reaching an 80–95% Hb level.

All patients suffered from ankylostomiasis, and some presented with haemoglobin levels as low as 15%. Detailed examination, including *x*-ray examination to exclude chest disease and peptic ulcer, showed no other disease. The treatment of the infestation was begun on admission and the intravenous iron therapy started on about the third day. No local or general reactions were noticed in the trial.—I am, etc.,

London N.2. H. A. LESLIE.

Reversed-ear Syndrome

SIR,—I was interested in Surgeon Lieutenant Antony Jarrett's paper (August 19, p. 483) on the reversed ear syndrome which may occur during diving in a frogman suit. Another manœuvre which, under certain circumstances, can produce barotrauma of the external auditory canal is positive pressure breathing. We have investigated the effects of delivering gas under pressure to the respiratory tract without applying counterpressure to the external auditory canal. The incidence of lesions in the canal is related to the magnitude and duration of pressure breathing. Thus no significant changes were seen at breathing pressures of less than 70 mm. Hg. Changes were produced in the majority of the subjects, however, by pressure breathing either at 80 mm. Hg for 20 minutes or 115 mm. Hg for 5–15 minutes. Typically the inner part of the canal and tympanic membrane were injected and covered with petechial haemorrhages and there was usually a fluid level in the middle ear. On several occasions a haemorrhagic bulla was present on the tympanic membrane.

Pressure breathing with trunk counterpressure increases the pressures throughout the cardiovascular system by an amount which virtually equals the imposed breathing pressure.[1] Thus the vessels of the lining of the external auditory canal are exposed to a similar increase of transmural pressure. Direct observation of the tympanic membrane and audiometry have shown that the pressure within the middle ear is only very infrequently increased during pressure breathing at high pressures. I agree, therefore, with Surgeon Lieutenant Jarrett that these lesions are vascular in origin and are not due to a rise of pressure within the middle ear cleft.—I am, etc.,

R.A.F. Institute of Aviation Medicine, Farnborough, Hants. J. ERNSTING.

REFERENCE

[1] Roxburgh, H. L., and Ernsting, J., *J. Aviat. Med.*, 1957, **28**, 260.

Advertising and Teenage Behaviour

SIR,—I was most interested to read the letter from Dr. Clifford Allen (May 13, p. 1392) and letters from Dr. Basil Merriman, Dr. John L. Tester, and Dr. John Playfair (June 10, pp. 1686–7). It is indeed a serious problem. It has been said, not without justification, that advertising is the only sphere in which we use our knowledge of psychology really intensively. It is called "market research," and utilizes primitive instincts, exacerbating jealousies, tensions, frustrations, prestige, and frank sexual lusts. There is certainly a connexion not only unforeseen by the youngster but tragically, in some circumstances deliberately, set. This is the connexion between drunkenness and promiscuity. There is a type of individual who deliberately encourages young girls to drink so that they may, to use a phrase I have heard too often, "get her to give what they want." It is this type of individual who is very likely to suffer from venereal disease.

On the question of smoking, as well as drinking, the advertisers create and develop the "teenage" images of what "teenagers" ought to do. It is not only that they make the young people want to be like somebody whose image they admire in the advertisement, but the romantic situation is exploited and drinking and smoking are subtly associated with being in love and romance. Ultimately, unconsciously, they drink and smoke to re-create an atmosphere. Finally, as a president of the

Brewers' Association in effect said before the war, their aim must be to see that the young people growing up became the mainstay of the public house.

It is not enough merely to appreciate these influences, something ought to be done about it. The Advertising Inquiry Council, 49 Cresswell Place, London S.W.10, has for several years past been trying to arouse public opinion. Support is badly needed, and the medical profession is in a position to give valuable leadership. The secretary will be only too pleased to give further information.—I am, etc.,

Farnham Royal, Bucks. M. E. M. HERFORD.

Post-operative Pneumoperitoneum

SIR,—Mr. P. Gilroy Bevan's two articles on pneumoperitoneum (September 2, pp. 605 and 609) raise points of great interest and importance to the abdominal surgeon, and we must feel considerably in his debt for them. He did not, however, in his researches cover the results of abdominal drainage, but it seems that this must introduce considerable additional risks, particularly in the clean case and in the upper abdomen. I am thinking of cholecystectomy and gastrectomy. Some surgeons are tempted to drain when not over-sure about the duodenal closure, and still more use this safeguard after an oesophago-jejunostomy, when the large space left by removal of stomach and spleen, coupled with the negative pressure under the diaphragm, must invite air entry in a big way. Should we not connect every upper abdominal drain, and perhaps lower abdominal as well, to an efficient under-water seal as we do with the pleural drain?—I am, etc.,

London W.1. STEPHEN POWER.

SIR,—Mr. P. Gilroy Bevan's paper (September 2, p. 609) concerning the relationship between post-operative pneumoperitoneum and pulmonary complications is interesting and stimulating. But I think it is worth noting that the relationship, as derived from Table IX of Mr. Bevan's paper, is not significant in the statistical sense.

The total incidence (i.e., major plus minor) of pulmonary complications is not significantly different in the two groups compared ($\chi^2=0.29$, $P>0.5<0.7$). The incidence of major complications is also not significant ($\chi^2=3.38$, $P>0.05<0.1$).

Furthermore, it would be generally agreed, I think, that such factors as the patient's age, sex, and whether or not he has respiratory disease influence the incidence of post-operative pulmonary complications. Mr. Bevan has not shown that his two groups were equal in these respects and it is therefore open to question whether they were in fact truly comparable.

In these circumstances it might be wise to await confirmation before accepting the full implications of Mr. Bevan's work.—I am, etc.,

Ashtead, Surrey. EDWARD THOMAS.

Fusion of Labia Minora

SIR,—In the correspondence columns of recent issues there have been mentioned instances of fused labia minora. In this hospital it is not infrequent to find instances of fused labia majora in infants and young girls, often referred to hospital as suffering from imperforate vagina.

Under anaesthesia to prevent discomfort to the children the fused labia can be separated just as readily as preputial adhesions can be released in the male. Within the fused labia the labia minora are found to be normal, relatively undeveloped, of course, at this age, and the vagina is normal. After release of the adhesions cleansing and lubrication is all that is required to prevent readhesion. Our most recent case was attended to on August 11.—I am, etc.,

Royal Hospital for Sick Children, Glasgow C.3. ANDREW P. LAIRD.

Shush!

SIR,—When a crying infant is shushed it often stops. This phenomenon is sufficiently a part of one's everyday experience not to require experimental or statistical verification. It is of interest since it is the first command that the child will obey.

Freud would probably have explained this by reference to an archetypical situation where mother and child exposed to some danger from a wild beast would suffer by natural selection if the child could not be silenced by a sound not differing greatly from the background. However, since it is possible to stop a dog's barking by the same means, this explanation is not so attractive as it seems at first sight.

It would appear, therefore, that the sound is as annoying to the child as to adults, so that the mood and its expression is self-perpetuating, often after the initial stimulus of pain or hunger is removed, and that this situation of positive feed-back can be stopped by injecting some noise into the system, and a sibilant, being a white noise, would be ideal for this purpose. It will be noted that this is a similar mechanism, but on an emotional basis, to the relief of stuttering by a rise in background noise.—I am, etc.,

Marlow Common, Bucks. D. B. JAMES.

Drug Advertisements

SIR,—Much is written about the control of information given to doctors about new drugs, the testing of new drugs and new combinations of old, and the control of advertisements in lay and professional journals.

I have seen no more pointed comment on this than is provided, unwittingly one must suppose, by two pages very near to each other in your issue of September 2. As I turned over the pages I read an editorial comment on page 659 that "lobidan" has been given a "short-term clinical trial" and that "it is doubtful if [the result obtained] is any better than might have been achieved by firm encouragement." I accepted that: but three pages later, advertisement page 26, I had to reject it because a half-page advertisement assured one that lobidan was "The pharmacological smoking deterrent" and that it had had "extensive clinical tests" which proved its efficacy.

You pay your money and take your choice? Perhaps: but the N.H.S. would have to bear a basic cost of 8s. 4d. if I accept the advertiser's words rather than those of yourself.—I am, etc.,

Kingston-upon-Thames, Surrey. D. STARK MURRAY.

Examination of Nurses

SIR,—Your annotation (September 2, p. 635) on the examination of nurses, commenting on Miss M. M. C.

Louden's letter (p. 648), smacks of the attitude of certain medical men who would strive to keep the nurses as ignorant as possible of the mystique of medical practice in order to maintain the veneration in which they wish to be held. Your comment on "the educational value of papers which would be well suited for a qualifying examination in medicine" makes it clear that you are not aware of the level of knowledge required in the answers to the questions quoted.

A doctor spends an average of about five minutes a day with each of his patients and then leaves the patient to be cared for by the nursing staff under the supervision of the ward sister or staff nurse for the remainder of the 24 hours. It is this care of the patient for the remainder of the 24 hours which is the subject of general nurse training and the examination which leads to State registration, which, in turn, is an indication that the nurse has gained the basic knowledge necessary for the performance of this task.

Can you imagine the waste of time and temper involved if every consultant or registrar had to explain to his ward sister every detail of treatment and management required for each patient? It is because the consultant knows that his ward sister is already equipped with a considerable knowledge of the particular diseases which affect his patients that he needs to add only the details of his own particular treatment. With the growing complexity of investigations and treatment which has occurred in recent years it is even more important now that nurses should understand what they need to observe, what they have to do, and why they have to do it. Knowledge of drugs and signs of overdosage and side-effects are equally important if nurses are not to go on giving drugs to the point of disaster before the signs are observed by the medical staff.

If your comments are representative of the opinion of the medical profession, which I very much doubt from my own contact with consultants who lecture to nurses, it would appear that you do not wish for informed, intelligent co-operation in the treatment of patients but demand that nurses remain the quiescent handmaidens of pre-registration days. As Miss Louden has so carefully pointed out, the position of State-enrolled nurse is open to those who will make good practical nurses but are not able to reach the standard required for registration or do not wish to accept the responsibilities of a ward sister's post.

In answer to your two questions, therefore, I would say: Yes, this "ordeal by examination" is unfortunately necessary in this age of paper qualifications to select those who are possessed of the basic knowledge to allow them to go on to the more responsible posts of ward sister and other appointments both inside and outside hospital. To the second question, "Is it being imposed by doctors from on high?," the answer is, No. It is the tutors who have pressed for these alterations, not the doctors or medical examiners.—I am, etc.,

B. J. SMITH,
Principal Tutor,
Royal Salop Infirmary Group Training School.
Shrewsbury, Salop.

Concurrent Intrauterine and Ectopic Pregnancies

SIR,—Dr. S. M. Feinberg (August 5, p. 385) describes a case of a normal pregnancy complicated by a concurrent ectopic pregnancy. I wish to report a similar case which presented in a different way.

The patient, a married woman now aged 35 years, had a normal pregnancy in 1954 and had since been healthy, but until this year had been unable to conceive again. Her last menstrual period began on January 20. On March 7 she was admitted to this hospital under the care of Mr. M. J. D. Noble with a history of vaginal bleeding and severe colicky abdominal pain. She was found to have guarding and extreme tenderness in the right iliac fossa, and a provisional diagnosis of ruptured tubal pregnancy was made. This was subsequently confirmed at laparotomy and it was noted that the uterus was only slightly enlarged. About a pint (0.6 litre) of blood and clot was removed from the peritoneal cavity and right salpingo-oophorectomy was performed. The patient made good post-operative progress and was discharged 10 days later.

On May 1 she was seen in the out-patient department and was very well. She had not menstruated since she left hospital and on vaginal examination the uterus was found to be the size of a 14-weeks pregnancy. The Hogben test was positive. This patient was seen again on June 12, when the uterus was enlarged to 20-weeks size and she reported having felt foetal movements. On July 29, when 27 weeks pregnant, she was again admitted with a history of a small, painless vaginal haemorrhage. Her blood-pressure was 140/90 and she had slight oedema. The signs of toxaemia have subsequently disappeared, but the patient has had five further episodes of loss of bright red blood per vaginam—only 1–2 oz. (28–56 g.) at a time. At the time of writing (August 25) the patient is quite well; the height of the fundus corresponds with the period of amenorrhoea (31 weeks); the head is presenting, but high; and the foetal heart is clearly audible.

It appears that this patient, who is herself a twin, began an intrauterine pregnancy and a tubal pregnancy at the same time and that the intrauterine pregnancy, though surviving the laparotomy at the sixth week, may be complicated by placenta praevia.—I am, etc.,

J. R. PERRY.
Marston Green Maternity Hospital and Hospital for Women, Nr. Birmingham.

Severely Subnormal Twins

SIR,—I am anxious to learn of any identical twins who are severely subnormal and inflict distressing injuries upon themselves. If any of your readers know of such cases, in which one or both twins are affected, I would be very interested to hear from them.—I am, etc.,

P. N. SWIFT.
Farnborough Hospital, Farnborough, Kent.

POINTS FROM LETTERS

Two Generations of Broken Homes

Dr. F. E. GRAHAM-BONNALIE (Exeter) writes: Having read Dr. C. J. Wardle's article "Two Generations of Broken Homes in the Genesis of Conduct and Behaviour Disorders in Childhood" (August 5, p. 349), I would like to draw attention to a common fallacy, whilst at the same time not in any way criticizing Dr. Wardle's findings. Whenever the question of difficult children is debated the argument which follows is almost inevitably centred around broken homes as being one of the chief factors, if not the chief factor, which produce difficult children. The result is that the broken home is too easily accepted as the fundamental cause, and the real causes are glossed over. Surely it is not the broken home but the reasons for the home becoming broken which produce the difficult children and hence the difficult adults. I suggest that the four main causes of difficult children are a lack of paternal love, a sense of insecurity, unpredictability in the parents, and an excess of love and care. In other words, it is the atmosphere of the home more than the breaking of it which is the source of the trouble.

Obituary

W. A. THOMPSON, M.R.C.S., L.R.C.P.

Dr. W. A. Thompson, one of Hull's oldest general practitioners, died on August 9 in his 83rd year.

William Atkin Thompson was born at Spilsby, Lincolnshire, on August 30, 1878, and studied medicine at Owens College, Manchester, qualifying in 1899. After holding a number of resident posts he came to Hull in 1907. There he became well known as a sympathetic and careful doctor who always took a great interest in his cases. Being a very competent obstetrician, he did a considerable amount of maternity work. In addition to his civilian medical work, Dr. Thompson had a distinguished Army career which began in the first world war. He was A.D.M.S. with the 50 Northumbrian Division and saw service in France and Belgium, commanding several field ambulance units, and he was with the 1/3 Northumbrian Field Ambulance, R.A.M.C., at Ypres along with the 4th Battalion East Yorkshire Regiment and other local units. Mentioned in dispatches, he also received the Médaille d'Honneur des Épidémies from the French Government. He was a former chairman of the Old Comrades' Association of the 1/3 Northumbrian Field Ambulance. With more than 20 years' service in the Territorial Army he was awarded the Territorial Decoration in 1924.

Dr. Thompson took a keen interest in the Jubilee Nursing Association and was a member of the committee for many years. Since the National Health Service came into being he had been a member of the Hull Jubilee Aid in Sickness Fund, and his work in this field will be greatly missed. He was medical officer to the Hull Kingston Rovers for many years and when he retired was made an honorary member of the club. An active member of the British Medical Association, he attended almost every meeting of the Branch and its social functions.

He is survived by his wife, a son, and two daughters, both of whom are in America.—I. G. I.

J. L. MARSHALL, M.B., B.Ch.

Dr. J. L. Marshall, who practised at Markethill, Co. Armagh, Northern Ireland, died after a short illness on July 21.

James Lister Marshall was born on May 28, 1899, a native of Northern Ireland. He was educated at Foyle College, Londonderry, and Trinity College, Dublin, where he graduated M.B., B.Ch. in 1925. In 1928, after the retirement of his father, Dr. Gilbert Marshall, from the position of dispensary medical officer at Markethill, he was appointed to the vacancy, and continued to practise there until the coming into operation of the Health Services Act in 1948. He then took service under the General Health Services Board, and remained in practice until his death. He was chairman of the old Portadown and West Down Division of the B.M.A. in 1936–7.

He is survived by his wife, son, and daughter, to whom our sincere sympathy is extended.

G. H. L. HAMMERTON, C.M.G., D.S.O.
L.R.C.P.&S.Ed.

Dr. G. H. L. Hammerton, who practised for many years in Dewsbury, died at his home in Hornsea, Yorkshire, on August 4. He was 86 years of age.

George Herbert Leonard Hammerton was born on March 2, 1875. He studied medicine at Sheffield and Glasgow, qualifying in 1900. He settled in Dewsbury after holding a resident post in the Dewsbury Infirmary, becoming police surgeon and medical superintendent of the borough's isolation hospital. He served with great distinction during the first world war, and was commanding officer of the 5th Cavalry Field Ambulance. Promoted to the rank of colonel, he was mentioned in dispatches four times, awarded the D.S.O. in 1917, and appointed C.M.G. in 1918. He returned to Dewsbury, and during the second world war was prominent in civil defence work. An enthusiastic supporter of the St. John Ambulance Brigade, he was county surgeon and later was appointed a knight of the Order of St. John of Jerusalem. He leaves a widow.

G. M. MUIRHEAD, M.B., Ch.B.

Dr. G. M. Muirhead died suddenly on August 14 at his residence, St. Nicholas Hospital, Gosforth, Newcastle upon Tyne. He was 63.

George Melbourne Muirhead was born in Glasgow in 1898, served in France and Flanders during the first world war in the Field Artillery, and graduated M.B., Ch.B. at Glasgow University in 1926. He had been assistant medical officer at Crichton Royal Hospital, Dumfries, and at Barnwood House, Gloucester, before coming to St. Nicholas Hospital in 1930, and when the National Health Service came into operation he was appointed senior hospital medical officer, in which capacity he was actively engaged at the time of his death.

His consistently equable and pleasant personality, sincere kindly interest, and quick apposite sense of humour soon endeared him to everyone at St. Nicholas, where patients and staff with increasing affection came to regard him as friend as well as doctor. All found him ever ready with kindly encouragement, advice, and help. He was a constant and stimulating participant in the various social and recreational activities, and as honorary secretary from its inception he played an important part in co-ordinating and developing these into the present flourishing social club organized for the benefit of all within the hospital. He loved his garden, and though he had little time to indulge this hobby he was an adept in the culture of flowers, obtaining superb results in great profusion, as many will gratefully remember.

Dr. Muirhead was an able clinician and a sound practical psychiatrist, quietly and unobtrusively devoted to his work in all its aspects. He was especially interested in children, and in recent years he had been developing with increasing success a rather unique application of psychiatry to children and their mothers within the *milieu* of a welfare clinic. He gave generously of his own time after formal out-patient sessions to many patients who will now greatly miss their occasional unappointed visits to him. Most of the rest of his leisure time was devoted to the British Red Cross Society, of which he was a life member, as medical officer of the Gosforth Detachment and assistant medical officer to the Northumberland Branch.

The very large cortège which overflowed the chapel at the cremation service on August 18 gave some indication of the affectionate regard in which Dr. Muirhead was so widely held. His familiar figure and cheerful presence will long be sadly missed by all at St. Nicholas, from whom and his many other friends deep sympathy is extended to his widow.—T. A. M.

ALICIA P. LINTON, M.B., B.S.

Dr. Alicia P. Linton (née Aldous), who was for many years a medical missionary in Persia, died in a London hospital on September 3. She was 83 years of age.

Alicia Pears Aldous was born at Dartmouth on June 19, 1878, the daughter of the Rev. J. C. Aldous, chaplain to H.M.S. *Britannia*. She received her professional training at the London (Royal Free Hospital) School of Medicine for Women, and graduated M.B., B.S. from London University in 1908. After working at the Canning Town Medical Mission she was sent by the Church Missionary Society to Persia in 1909 as junior surgeon at the Women's Hospital, Ispahan. In 1910 she married the Rev. J. H.

Linton, who was subsequently Bishop of Persia from 1919 to 1935, and, later, Assistant Bishop of Birmingham. Their long period of work in Persia was a notable example of a husband-and-wife partnership in the service of the Church overseas.

Dr. Linton returned to England during the first world war, and from 1917 onwards was senior house-surgeon at Northampton General Hospital. In 1921 she went back to Ispahan as senior surgeon at the Women's Hospital and remained there until 1932. During the second world war she worked as a medical officer at clinics in Birmingham. Her husband predeceased her in 1958. They had four sons and one daughter, their eldest son being killed in the evacuation of Crete while serving with the R.A.F.

R. MARKHAM CARTER, C.B., F.R.C.S., D.T.M.

The obituary of Lieutenant-Colonel R. Markham Carter was published in the *Journal* of March 25, 1961 (p. 908).

Dr. P. V. GHARPURE writes from Grant Medical College, Bombay: While Colonel Carter worked as physician in the Sir Jamshedjee Jeejeebhoy Hospital in Bombay I worked under him in 1923–4. I recollect his firm attitude to all problems and his keen sense of duty. He admired good work and always expressed his appreciation. He had the most sympathetic feelings towards patients. He worked in the twin institutions—J. J. Hospital and the Grant Medical College—in many capacities, leaving the stamp of his work on anything he handled. As one who had close associations with him I pay my tribute to his memory.

Mr. W. J. BISHOP

The obituary of Mr. W. J. Bishop was published in the *Journal* of August 5 (p. 389).

Dr. W. R. BETT writes from New York: My friend and colleague for 37 years, "W. J." was so full of life, fun, energy, and plans for the future that it is hard to think of him as no longer with us. Though he was always in a hurry, he liked to pause for a chat, a joke, an anecdote. With a facile pen and an exceedingly readable style he combined a scholar's conscience in consulting the original sources, and these sources he knew where to find. Courteous, and modest to a fault, he could be an outspoken critic and a strict disciplinarian where slipshod work was concerned. His contacts and friends were many and distinguished on both sides of the Atlantic and on the Continent. He walked with the kings of the profession, yet lost not the common touch. He shared J. D. Rolleston's Rabelaisian humour and his illustrious brother's urbane erudition. My most vivid memory of "W. J." will always be seeing him almost precipitately rushing up on the stage when invited by the chairman to speak—with the enthusiasm of the youthful Sophocles leading the chorus of victory after the battle of Salamis.

RAFFAELE BASTIANELLI, M.D., Hon.F.R.C.S.

The obituary of Professor Raffaele Bastianelli was published in the *Journal* of September 9 (p. 714).

Dr. E. GREY-TURNER writes: My father first met Professor Bastianelli in 1918, when they were colleagues (with George E. Gask, Pierre Duval, and others) in an allied surgical mission which visited the United States to tell American surgeons what the Allies had learned about war surgery. They became firm friends and remained so from that time till my father's death ten years ago. I recall a snapshot that always hung on the wall of my father's bedroom showing my parents with Bastianelli on the occasion of the Congress of the International Society of Surgery in Rome in 1926. At one of the ceremonies connected with that congress an attempt was made on the life of Mussolini, and Bastianelli then left Rome in professional attendance upon the dictator.

My own first meeting with Bastianelli was in 1944. Shortly after the capture of Rome I called at 2 Via dei Vellini and presented the compliments of my family to the Professor and his wife. (On the same visit to Rome I called also on Professor Margharucci, who introduced me to his son, a charming lad who, alas, was killed a few months later fighting with Italian troops on the side of the Allies.) Bastianelli and his wife received me very warmly, and he told me without a trace of bitterness that the Allies had taken him into custody for a few days because Mussolini, as a mark of distinction, had made him a senator.

My last meeting with Bastianelli was in 1951, just after my father's death, when he and his wife, with great sympathy and kindliness, entertained my mother and me for a short holiday at their lovely villa near Florence. Although he was nearly 90 he was as alert and stimulating as a man half his age. He recalled as a small boy seeing the troops of Napoleon III in Rome, guarding the Pope. He told me of his mountaineering adventures and of his experiences flying his private aeroplane. He bought his first plane at Hatfield from De Havillands in the early days of flying, crashed it just after take-off, and immediately bought another. He talked about King Vittorio Emmanuele, and about Mussolini, both of whom he had attended regularly. Above all he took the keenest pleasure in motoring us round his vineyards and his estate, where he—brilliant surgeon, intrepid mountaineer, and aviator—was a country squire, and relished it.

Medico-Legal

TRANSFER TO MENTAL HOSPITAL OF PRISONERS COMMITTED FOR CONTEMPT

[FROM OUR LEGAL CORRESPONDENT]

In an application to Mr. Justice Salmon on July 14 a lacuna in the Mental Health Act, 1959, was revealed *(Pearson v. Stuart)*. In this case the defendant had been committed to prison for contempt of court by her breach of a civil injunction. She was not certifiable when originally before the court, but while in prison it became apparent that she ought to be transferred to a mental hospital. Sections 72–78 of the Act empower the transfer to hospital, by order of the Home Secretary, of several categories of prisoner. Although one of those categories consists of "civil prisoners," the definition of such prisoners is limited to persons "committed by a court to prison for a limited term." Persons committed for contempt of court are committed to prison for an unlimited term and so do not fall within any of the categories listed. At the request of the Official Solicitor, an order was made for the prisoner to be released on July 15 so that independent arrangements could be made for her transfer to hospital.

Vital Statistics

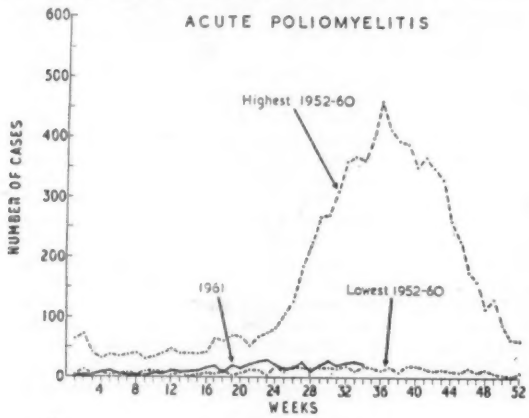
Infectious Diseases

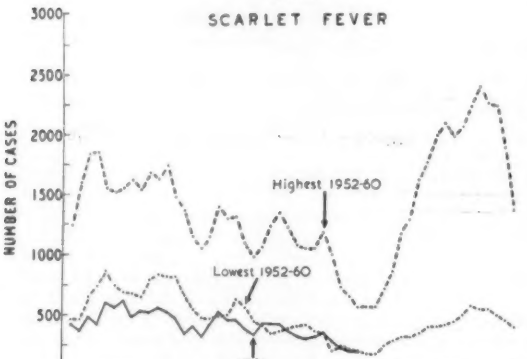
Areas where the numbers of notifications were high in the latest two weeks for which figures are available.

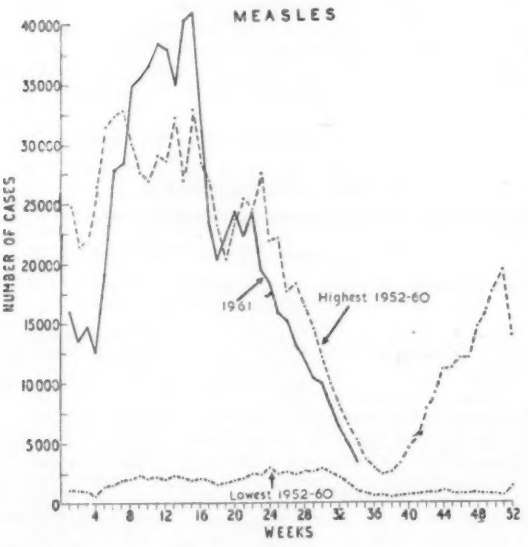
	Week Ending Aug. 26	Week Ending Sept. 2
Dysentery		
Staffordshire	11	**21**
Stoke-on-Trent C.B.	5	**18**
Yorkshire, West Riding	22	**37**
Worsbrough U.D.	1	**16**
Glasgow	78	**90**
Food-poisoning		
Lancashire	282	**815**
Blackpool C.B.	253	**752**

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1952–60 are shown thus ------, the figures for 1961 thus ———. Except for the curves showing notifications in 1961, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.







INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **August 26** (No. 34) and corresponding week 1960.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the whole of England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1961					1960				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria ..	3	0	1	0		1	0	2	0	1
Dysentery ..	242	46	152	9	9	296	29	159	6	8
Encephalitis, acute	3	0		0		1	0	0	0	
Enteric fever:										
Typhoid ..	4	0	0	0		3	0	0	0	
Paratyphoid ..	4	0	1 (B)	0		8	0	0	1	
Food-poisoning ..	428	21	20	3		190	20	31	2	
Infective enteritis or diarrhoea under 2 years				12	26				11	24
Measles*	3,479	107	11	22	7	1,613	80	31	3	12
Meningococcal infection	18	0	8	0		14	2	18	2	1
Ophthalmia neonatorum	20	2	2	0		23	2	3	0	
Pneumonia† ..	112	10	79	1		158	10	98	0	1
Poliomyelitis, acute:										
Paralytic ..	14	0	0	0	1	10	3	0	1	6
Non-paralytic ..	7	0	1			9	0	0		
Puerperal fever§ ..	164	31	17	2	1	154	30	23	2	
Scarlet fever ..	179	13	22	12	2	188	7	26	5	18
Tuberculosis:										
Respiratory ..	299	37	53	13		381	44	82	12	
Non-respiratory	42	6	7	13		56	1	13	2	
Whooping-cough	290	9	37	12	14	1,467	149	116	0	20

DEATHS	1961					1960				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria ..	0	0	0	0	0	0	0	0	0	0
Dysentery ..	1	0		0		2	0		0	
Encephalitis, acute		0			0		0			0
Enteric fever ..	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	7	0	1	0	0	4	0	1	1	0
Influenza	4	0	0	0	0	4	0	0	0	0
Measles		0	0	0	0		0	0	0	0
Meningococcal infection		0	0				1	1		
Pneumonia ..	374	25	14	8	4	391	34	13	17	10
Poliomyelitis, acute	2	0		1	0	2	0		0	0
Scarlet fever ..		0	1	0	0		0	0	0	0
Tuberculosis:										
Respiratory ..	47	2	5	0	0	55	3	6	1	1
Non-respiratory		2		0	0		1	0	0	0
Whooping-cough	0	0	0	0	0	2	0	0	0	0
Deaths 0–1 year ..	268	41	28	11	8	271	30	26	11	19
Deaths (excluding stillbirths) ..	8,326	685	520	98	126	8,770	705	558	122	162
LIVE BIRTHS ..	15,456	1353	1009	274	445	14,562	1280	968	276	406
STILLBIRTHS ..	297	23	26			305	28	27		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

B.M.A. Luncheon for B.A.'s President

On September 4 members of the Norwich Division of the British Medical Association entertained Sir WILFRID LE GROS CLARK, F.R.S., President of the British Association for 1961, to luncheon in Norwich. Proposing the health of the British Association's President, Dr. G. S. BARRADELL-SMITH, chairman of the Norwich Division, said that there was a probably unique feature of this year's meeting of the B.A.: with Sir Wilfrid as President, Sir GEORGE ALLEN as secretary, and Mr. MICHAEL BULMAN as chairman of the local executive committee, three of its most important functionaries were medically qualified.

Ireland Honours Surgeons

Several distinguished surgeons were honoured during the Congress of the International Society of Surgery and the International Cardio-vascular Society, which took place in Dublin from September 2 to 9. The Royal College of Surgeons in Ireland conferred honorary fellowships on the president of the Congress, Professor E. DAHL-IVERSEN (Copenhagen), Dr. ALTON OCHSNER (New Orleans), and Professor CLARENCE CRAFOORD (Stockholm). The M.Ch. *honoris causa* of Dublin University was conferred on Professor PAUL MARTIN (Brussels), Professor C. G. ROB (Rochester, New York), Professor JOA AFFONSO CID DOS SANTOS (Lisbon), and Professor PIERRE WERTHEIMER (Lyons). The National University of Ireland bestowed the honorary degree of M.Ch. on Professor LAMBERT C. ROGERS (Cardiff), Professor F. D. MOORE (U.S.A.), Professor FRITZ LINDER (Berlin), Dr. FERNANDO MARTORELL (Barcelona), Dr. F. L. A. GERBODE (San Francisco), Professor PIETRO VALDONI (Rome), and Professor R. E. L. DANIS (Brussels). The Royal Academy of Medicine admitted to honorary fellowship Mr. H. WARDELL S. WRIGHT (London), Dr. H. HAIMOVICI (New York), Professor G. ARNULF (Lyons), and Professor HEINZ BUERKLE DE LA CAMP (Munich). (See also p. 762.)

Chair of Pharmacology, St. Bartholomew's Hospital

Dr. J. P. QUILLIAM, reader in pharmacology at St. Bartholomew's Hospital Medical College, has been appointed to the University of London chair of pharmacology tenable there.

Dr. Quilliam qualified M.B., B.S.(Hons.), M.R.C.S., L.R.C.P. from University College Hospital in 1941, and held posts there and at the Brompton Hospital until he became experimental officer at the Chemical Warfare Experimental Station in 1942. He served in the Medical Branch of the Royal Air Force from 1943 to 1946. From 1946 he was lecturer at King's College, London, then from 1948 to 1956 was part-time lecturer in pharmacology at Bart's Medical College, and senior lecturer in charge from 1956 to 1958, when he became university reader. In 1949 he was the London University British Postgraduate Medical Federation Travelling Fellow at Johns Hopkins Hospital, Baltimore. His research since the war has been directed towards the study of the mode of action of centrally active drugs at inter-neuronal sites such as the synapses in the superior cervical ganglion, using both traditional and electrical methods.

Royal College of Surgeons of Edinburgh

The Royal College of Surgeons of Edinburgh, founded by James IV in 1505, has been in its present Surgeons' Hall, designed by W. H. Playfair, since 1832. Virtually unchanged since additions in 1908, the Hall could no longer adequately house its administrative offices, its library, its museum, or even the editor of its journal, and it had no council room. Under the scheme of reconstruction and expansion which has recently been completed the offices of the college and of the Central Midwives Board have now been moved to a neighbouring building in Hill Square, and a modern business entrance of teak and glass has been provided. The formal and business parts of the college are linked to each other and to the new entrance by a restored corridor. A long vaulted reading-room has been formed from three offices, and a council room carved out of the Central Midwives Board's former office and a store-room. The main museum, which is one of Playfair's finest interiors,

[*Studio Seven, Glasgow*

The restored corridor in Playfair's building, with the vista to the main staircase revealed and portraits by Sir John Medina. The chandelier is of modern Waterford crystal.

remains more or less as he planned it. Cloakrooms and library storage have been created in the hitherto unused basement of the main building, and editorial offices in the remodelled basement at Hill Square. (*Scotsman*, August 24.)

Survey of Tanganyika's Medical Needs

A survey, financed by the African Research Foundation and supported by the Tanganyikan Government, is shortly to be carried out in Tanganyika. Its findings will be used in planning the development of the country's health services. The survey report will be made by Professor R. M. TITMUSS (London School of Economics), Professor G. MACDONALD (London School of Hygiene and Tropical Medicine), and Dr. A. W. WILLIAMS (director of postgraduate medical studies, University of Oxford). Dr. C. WOOD (London School of Hygiene and Tropical Medicine) and Dr. ABEL SMITH (London School of Economics) will visit the Territory for three weeks to collect preliminary facts and figures. It is hoped that the report will be ready early in the new year.

Royal Society of Medicine

The Royal Society of Medicine, which is becoming increasingly cramped in its present quarters, would like to acquire the site of the Western District Post Office immediately next door when the Post Office authorities abandon it in a few years' time, and the society is negotiating to this effect. In the meantime part of the R.S.M.'s basement is being converted into rest-rooms and changing-rooms, and the building of an office unit on the roof is being considered. Thereafter the society's most pressing needs would be for bedrooms, extra storage space for books and journals, for offices for the photographic unit in 1969 if its present lease cannot be extended, for a meeting-hall seating 500 people, and for reading accommodation for non-members of the society. (*Annual Report of the Council 1960–1961.*)

The London Honours Famous Men

The London Hospital has erected two plaques on London houses, each to commemorate a London Hospital doctor—James Parkinson (1755–1824) and William J. Little

(1810–1894). The plaques were unveiled on August 1, Parkinson's by his great-great-grandson, Dr. R. TRINGHAM, a family doctor practising in Norwich, and Little's by his grandson, Admiral Sir CHARLES LITTLE.

James Parkinson was the son of a doctor living in Hoxton Square, Shoreditch. The house was demolished about 40 years ago and replaced by a furniture factory on which the plaque has been placed. He was a pupil of an assistant surgeon at the London, and is remembered for his classical description of paralysis agitans, or Parkinson's disease. He was an able geologist and palaeontologist, a radical, a reformer, a political agitator, and a pamphleteer. No portrait of him has ever been found, but a friend describes him as being "rather below middle stature, with an energetic, intelligent, and pleasing expresssion of countenance." W. J. Little was born in Aldgate at the Red Lion Inn, where his father was landlord. To-day a later building of the same name stands on the site in Leman Street, and the plaque has been placed on it. He studied medicine at the London and qualified as a doctor. He was the first to investigate the cause of spastic rigidity of the limbs of newborn children, and the name of Little's disease, or spastic diplegia, has been given to these disabilities. (Photograph of W. J. Little by courtesy of Dr. D. Hunter.)

Royal Medical Benevolent Fund

During 1960 the Royal Medical Benevolent Fund made grants amounting to £34,438, an increase of £2,733 on 1959; £14,197 was paid out in annuities, £622 more than the year before. During the year £6,500 in income tax was recovered through seven-year covenants, and 233 new covenants were signed. The aim of the fund is to help all suitable members of the medical profession and their dependants, and it would welcome more subscribers, particularly from among the younger members of the profession. Its address is 37 St. George's Road, Wimbledon, London S.W.19 (Telephone: Wimbledon 1792). At the annual general meeting Sir ZACHARY COPE was elected president, Mr. G. H. BATEMAN honorary treasurer, and Dr. T. ANWYL-DAVIES honorary secretary.

Rudolph Steiner Centenary

Lectures, films, and a centenary exhibition were given at Rudolph Steiner House on September 8 and 9 to illustrate the work of the specialized schools and homes which are run in accordance with the methods of Rudolph Steiner and which deal with every type of defective, maladjusted, and delinquent child. The exhibition included glass engraving, pottery, and drawings, as well as "sculptures" done by blind children at the Camphill Schools.

New D.S.I.R. Headquarters

The headquarters of the Department of Scientific and Industrial Research has moved to State House, High Holborn, London W.C.1. (Telephone: CHAncery 1262.)

People in the News

▶ Major-General J. C. BARNETSON has succeeded Major-General W. A. ROBINSON as Deputy Director-General Army Medical Services.

▶ Mr. F. W. LAW has been appointed honorary consultant in ophthalmology to the Army in succession to Sir STEWART DUKE-ELDER, F.R.S., who has retired.

COMING EVENTS

Anglo-German Medical Society.—Symposium, "Drug Action and Modern Therapy," September 28–30, Royal Society of Medicine, 1 Wimpole Street, London W.1. Subjects: "The Oral Antidiabetic Agents"; "Anabolic and Gestational Steroids"; "Modern Drugs Used in Psychiatry"; "Side-effects of Drugs." Non-members admitted by ticket from Honorary Secretary, Dr. E. KAWERAU, Department of Chemical Pathology, St. James' Hospital, Balham, London S.W.12.

Exhibition, "Medical Disposable Products."—Sponsored by Lewisham Division, British Medical Association, October 3 (2–6 p.m.), October 4 and 5 (10 a.m.–6 p.m.), Grove Park Hospital, Marvels Lane, London S.E.12.

National Society for Clean Air.—Annual conference and exhibition, Brighton, October 4–6. Details from N.S.C.A., Field House, Breams Buildings, London E.C.4.

British Biophysical Society, Biochemical Society.—Joint meeting at School of Pharmacy, Brunswick Square, London W.C.1. British Biophysical Society, "The Physical Chemistry of Phospholipids," October 5, 11 a.m.; Biochemical Society, "Phospholipids and Sulpholipids," October 6, 10.30 a.m.; ordinary meeting at Westminster Medical School, October 7, 10 a.m. Details from Dr. W. J. WHELAN, Lister Institute of Preventive Medicine, Chelsea Bridge Road, London S.W.1.

7th Congress of International Union of Therapeutics.—Geneva, October 6–8. Details from Secretariat, Case 229, Geneva 4, Switzerland.

Institute of Diseases of Chest.—Clinical demonstrations, open to medical practitioners without fee, arranged by Dr. J. SMART, in Institute's lecture-room (in grounds of Brompton Hospital, Fulham Road, London S.W.3). Fridays at 5 p.m., October 6–December 15, inclusive.

College of General Practitioners.—Annual symposium, "The Training of the Family Doctor for His Work in the Community." Discussions: "Undergraduate Training" (chairman: President of College), "The Training of the Young Doctor" (chairman: Sir JAMES PATERSON ROSS), November 26, Wellcome Building, Euston Road, London N.W.1. Tickets from Secretary of College, 41 Cadogan Gardens, London S.W.3.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Tuesday, September 19

●INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Hammersmith Hospital, 3 p.m., Professor D. B. Stewart (West Indies): Infectious Granulomata of the Female Genital Tract.

ROYAL ARMY MEDICAL COLLEGE.—5 p.m., Professor M. L. Rosenheim: Investigation of Hypertension.

Wednesday, September 20

●INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Chelsea Hospital for Women, 3 p.m., Professor D. B. Stewart (West Indies): Advanced Extra-uterine Pregnancy.

Thursday, September 21

GROUP FOR REPRESENTATION OF THE VIEWS OF CLINICAL PSYCHIATRISTS.—At Rygate Room, Tavistock House North (Fourth Floor), Tavistock Square, W.C., 5.30 p.m., committee meeting

INSTITUTE OF NEUROLOGY.—(1) 3.30 p.m., Professor Elizabeth Roboz-Einstein (California): Biochemical Approach to Multiple Sclerosis and Allergic Encephalomyelitis. (2) 5.30 p.m., Dr. G. von Békésy (Harvard): Lateral Inhibition in the Skin, the Ear, and the Eye.

SOCIETY OF MEDICAL OFFICERS OF HEALTH: HOME COUNTIES BRANCH.—11.30 a.m., visit to Carreras Ltd., Basildon, Essex.

Friday, September 22

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. F. H. Scadding: clinical demonstration.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Searle.—On September 5, 1961, at the North Devon Infirmary, Barnstaple, to Dr. Gwen Searle (formerly Edwards), wife of Dr. J. S. T. Searle, a sister for Anne and Corinne.

DEATHS

Barber.—On August 26, 1961, at his home, 8 Seaway Avenue, Christchurch, Hants, Alec Barber, M.B., B.S., D.P.H.

Boyd.—On August 20, 1961, at Edinburgh, Gladys Annie Adeline Boyd, M.B., Ch.B., D.P.H.

Cameron.—On August 16, 1961, at Dall Lodge, Killin, Perthshire, John Allan Munro Cameron, M.D.

Edmiston.—On August 24, 1961, John Francis Edmiston, T.D., M.B., Ch.B., of Great Shelford, Cambs.

Godfrey.—On August 21, 1961, Maurice Arthur Godfrey, L.R.C.P.&S., L.D.S. R.C.S Ed., of 4, Ripon Road, Harrogate, Yorks, aged 52.

Wallace.—On August 25, 1961, at his home, West Hatch, Som., Herbert Smith Wallace, M.B., Ch.B., late of Nottingham.

Any Questions ?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Measuring Fall-out

Q.—*Is there a cheap reliable instrument for detecting radioactive fall-out?*

A.—When the activity of nuclear test debris is small elaborate and costly apparatus, operated by skilled personnel, is required for detecting and measuring radioactive fall-out. In fact, certain aspects of the fall-out monitoring programme have always presented difficult technical problems, even during the period of maximum deposition which occurred in April, 1959. For example, there has always been considerable interest in the assessment of caesium-137 and strontium-90 because they are the two radio-nuclides in fall-out which are present to any extent in animals and humans, and the problem has been to measure their activities against a background of more active components of the fall-out which emit similar radiations. In the case of caesium-137, which is a beta- and gamma-emitter, the estimations are usually made with a calibrated gamma-ray spectroscope costing at least hundreds and often thousands of pounds. For the accurate estimation of strontium-90, which is a pure beta-emitter, elaborate chemical separations, carried out in laboratories specially designed to prevent cross-contamination with other beta-emitters, are required before counting the specimens in complicated, low-background Geiger-counter assemblies.

However, in 1958 and 1959, when the fall-out rate was greatest, a measurement of the total gamma radiation from nuclear test material on the ground could have been accomplished with simple and relatively cheap apparatus. For example, Spiers[1] and Vennart[2] have described measurements of the increases during that period in the local gamma-ray background due to the testing of nuclear bombs. Spiers used a high-pressure ionization chamber of his own design. Vennart used commercially available Geiger tubes and electronic equipment. The cost of a suitable Geiger tube is about £3 and of the power supplies and counter £100 to £300. It is important to note, however, that such measurements have to be interpreted with care. Even at the peak period of deposition, fall-out increased the count rate of the Geiger counter used in Vennart's measurements by only about 50% above that due to cosmic rays and the natural gamma-ray background. It was necessary therefore to determine the count rate due to these two natural sources of radiation during a period of negligible fall-out.

Any increase in the amount of fall-out above that reported for 1959 would obviously make its detection easier. Indeed, during certain circumstances there might be no need to use instruments as sensitive as high-pressure chambers and Geiger counters. In this respect it is worth noting that Spiers[1] and Vennart[2] both reported that, at its maximum, the dose rate at the earth's surface due to gamma rays from fall-out amounted to about 25 mrads/year. However, after an accident at an atomic energy establishment, the doses recommended by the Medical Research Council[3] as acceptable for members of the public are 20 to 30 roentgens of gamma rays measured in air. Radioactive fall-out giving rise to doses of this magnitude in a few hours, days, or even weeks could be detected and measured with fountain-pen-sized dosimeters of the quartz fibre type. The price of one of these instruments is about £8 and the charging unit, which serves any number of dosimeters, about £13. Alternatively, it might be possible to use sensitive photographic film if time was available for its development and processing. Suitable film costing a few pence per piece is now manufactured which will record doses ranging from a few milli-roentgens to several hundred roentgens of gamma radiation.

From the foregoing it will be clear that the cost and complexity of an instrument which will detect radioactive fall-out is very dependent on the amount of radioactivity concerned and upon whether information is required about its composition.

REFERENCES

1 Spiers, F. W., *Nature (Lond.)*, 1959, **184**, 1680.
2 Vennart, J., ibid., 1960, **185**, 722.
3 *The Hazards to Man of Nuclear and Allied Radiations*, Appendix K, 1960. H.M.S.O., London.

Anaemia in Chronic Nephritis

Q.—*What is the relation of the anaemia of chronic nephritis to the raised blood urea?*

A.—The development of anaemia in chronic nephritis is closely related to the degree of nitrogen retention in the blood, and when the urea is raised to 100 mg. per 100 ml. or more for any length of time anaemia develops. The main cause for this anaemia is suppression of bone marrow activity. It seems unlikely that the urea itself is responsible, and there is increasing evidence that a factor(s) is secreted by the kidney which influences erythropoiesis. Seriously damaged kidneys do not secrete this factor in adequate amounts, and anaemia occurs when the renal damage is sufficient to raise the blood urea to 100 mg. or more.

Furunculosis of Ears

Q.—*A healthy woman aged about 44 years has been suffering intermittently for several years from severe furunculosis in one or both ears, which has obstinately resisted all forms of treatment. How should this condition be dealt with?*

A.—Investigation of the general health is important: it is wise to test the urine, particularly for sugar, to regulate the diet and correct excessive carbohydrate or possibly fat intake, and to inquire into the patient's mode of life and emotional state. Swabs may be taken from the nares or other moist areas of the skin to determine if there is any carriage of staphylococci. If found, treatment with an ointment containing neomycin or bacitracin is worth a trial. Persistent otitis externa may follow an attack of furunculosis and predispose to further bouts. It may be associated with seborrhoea of the scalp. This should be treated for a long period, since it is likely to lead to relapse of the otitis. Otitis externa may be caused by an underlying otitis media possibly with only a small marginal or attic perforation and scanty discharge from the middle ear. To allay the irritation caused by otitis externa, the patient may scratch the ear with the finger-nail or some instrument inserted into the meatus and cause another furuncle. Initially the otitis externa may be treated with an ointment containing a broad-spectrum antibiotic such as neomycin and hydrocortisone in a non-greasy base. Subsequently the meatus should be painted with 2% crystal (gentian) violet in 50% alcohol/water at weekly or longer intervals, and thereafter inspected at monthly intervals to ensure that the skin remains dry and healthy. Some otologists consider that systemic antibiotics should not be given routinely. Although the furuncle under treatment will respond, another attack is more likely to occur a few weeks later, because, owing to the antibiotic, the patient's immunity reaction has not received such a strong stimulus.

Choosing a Tetracycline

Q.—*Assuming that the causative organism of an infection is sensitive (by paper disk method) to tetracycline, oxytetracycline, and chlortetracycline, is there any practical therapeutic difference between these three? Is there any advantage in giving nystatin in addition when the treatment does not exceed five days?*

A.—There are slight differences in the susceptibility of some species of bacteria to different tetracyclines—e.g.,

pneumococci and staphylococci are more susceptible to chlortetracycline than to tetracycline or oxytetracycline, and *Pseudomonas pyocyanea* is usually more susceptible to oxytetracycline than to the other two. There are also differences in the levels attained in the blood and the degree of penetration into the cerebrospinal fluid which somewhat favour tetracycline. Thirdly, there are said to be differences in liability to cause side-effects which again favour tetracycline. The questioner does not mention demethylchlortetracycline: this has in general a higher antibacterial activity than any of the other three and is more slowly excreted, with the result that adequate concentrations can be maintained in the blood with smaller or less frequent doses. The fifth day is about the time when superinfection with *Candida albicans* may first become manifest during treatment with a tetracycline. If it is known that the course is unlikely to exceed five days, it seems scarcely worth while to administer nystatin as well from the beginning: it can always be given later should any symptoms of *Candida* infection develop.

Prolonged Use of Amphetamines

Q.—*A middle-aged woman has been taking dexamphetamine sulphate and amylobarbitone combined, in the form of "drinamyl" tablets, one twice daily, for a year. Would it be harmful for her to continue on this dosage indefinitely, or should she be put on some preparation without amphetamine?*

A.—A recent leading article in the *Journal*[1] stated that preparations containing small doses of the amphetamines with a barbiturate have a place in the treatment of the milder forms of depression, though a tendency to addiction is a worrying feature. True addiction to the amphetamines probably does not occur, but there is no doubt that patients do become both tolerant and habituated to them. With this exception, there would appear to be no particular reason why this preparation should not be continued indefinitely. Cumulative side-effects from the long-term use of dexamphetamine in therapeutic doses are rare.[2] Leake[3] comments that clinical experience has abundantly confirmed laboratory studies that the amphetamines are relatively safe and that dexamphetamine is the one with the greatest safety margin. He quotes instances in which dexamphetamine has been given in therapeutic doses for as long as nine years without any ill effect. It should be appreciated, however, that when used in this way—i.e., in a small dose continuously—dexamphetamine is being used more as a psychological crutch than for any pharmacological effect, which is probably no greater than that of an additional cup of strong tea or coffee.

REFERENCES
1 *Brit. med. J.*, 1960, **1**, 178.
2 Ibid., 1955, **1**, 679.
3 Leake, C. D., *The Amphetamines*, 1959. Charles C. Thomas, Springfield, Ill.

Nylon Hairbrushes

Q.—*Is the use of nylon hairbrushes harmful to the hair?*

A.—Dr. Agnes Savill drew attention[1] to the effect of nylon brushes on the hair. Brushing with nylon brushes can have the effect of pulling some hairs out by the roots and of breaking others and fraying their ends. Since Dr. Savill drew attention to this condition most dermatologists have seen cases both in men and women where loss of hair has followed the vigorous use of a nylon brush. Sometimes, as a result of the loss of hair, the brush is plied even more vigorously for its supposed beneficial effect, but only to aggravate the condition. Once the nylon brush is discarded and the old-fashioned bristle brush used in its place, the hair may be expected to grow again.

REFERENCE
1 Savill, A., *Brit. J. Derm.*, 1958, **70**, 296.

NOTES AND COMMENTS

Inheritance of Albinism.—Dr. I. F. ANDERSON (Johannesburg) writes: In the "Any Questions?" section of the *Journal* (April 15, p. 1121) the inheritance of albinism is discussed. The bold statement is made that this recessive condition is not associated with any diminution of intelligence. It has been my impression, and I see that Fraser Roberts agrees,[1] that albinos manifest with mental deficiency somewhat more commonly than the general population. This probably somewhat remote association is worth bearing in mind when giving "genetic" advice to parents.

OUR EXPERT replies: I am grateful for Dr. Anderson's comment, which I find is a fairly widespread impression, but one which my own experience has not supported. It would not be surprising if there was an association sometimes of a gene producing mental abnormality with that for albinism. Dr. Fraser Roberts[1] gives no reference to support his statement that albinos manifest mental deficiency more commonly than the general population. Sorsby[2] does not mention the relationship, but Cockayne[3] quotes a number of instances of imbecility among the siblings of albinos. I have not been able so far to find any statistical evidence of the relationship of albinos and mental retardation, nor do albinos seem to find their way into institutions for the mentally subnormal more than very rarely. I wonder whether this impression has perhaps been caused by the educational retardation resulting from poor eyesight and deafness in some albinos.

REFERENCES
1 Fraser Roberts, J. A., *An Introduction to Medical Genetics*, 1960. Oxford University Press, London.
2 Sorsby, A., *Clinical Genetics*, 1953. Butterworth, London.
3 Cockayne, E. A., *Inherited Abnormalities of the Skin and Its Appendages*, 1933. Oxford University Press, London.

Anaesthesia for Manual Removal of Placenta.—Dr. A. MACKENZIE (Department of Anaesthetics, Royal Victoria Infirmary, Newcastle upon Tyne) writes: I find the last paragraph of your reply to the query about anaesthesia for manual removal of placenta ("Any Questions?" May 20, p. 1477) rather difficult to understand. If my interpretation of it is correct, however, it seems to me that the administration of morphine gr. ¼ (16 mg.) intravenously to a patient in severe haemorrhagic shock could be a very hazardous proceeding, particularly in the absence of adequate resuscitative equipment, which is implied. There are two great advantages of using the intravenous route in these circumstances: first, the certainty of absorption; and, secondly, the ability, given time and adequate dilution of dosage, to administer *enough* rather than a set dose which must be a guess. Having encountered respiratory and circulatory depression of sufficient degree to warrant artificial respiration and active resuscitation after the intravenous administration of pethidine 100 mg. during labour to an otherwise fit patient, I am prompted to make this point.

Corrections.—In his article "Neonatal Tetanus in Sierra Leone" (June 17, p. 1721) Dr. J. L. Wilkinson, referring (p. 1723) to approximate dosage of chlorpromazine given, should have written "approximately 22 mg./kg. (10 mg./lb.) to start with, declining to 11 mg./kg. (5 mg./lb.) daily later, in divided doses."

In the "To-day's Drugs" comment on long-acting sulphonamides (September 9, p. 704) once-daily dosage was suggested. For sulphaphenazole ("orisulf") this should have been twice-daily dosage (*Supplement to the Extra Pharmacopoeia*, 1961).

Collected Articles from the "British Medical Journal"

The following books are available through booksellers or from the Publishing Manager, B.M.A. House. Prices, which include postage, are now the same for both inland and overseas.

Drugs in the Treatment of Disease (36s. 9d.).
Refresher Course for General Practitioners, Volume 3 (26s. 9d.).
Any Questions?, Volume 3 (8s. 3d.).

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